ANNALS
OF THE
RHEUMATIC DISEASES

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The Official Journal
of the
EMPIRE RHEUMATISM COUNCIL

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ANNALS

OF THE

RHEUMATIC DISEASES

THE OFFICIAL JOURNAL OF

THE EMPIRE RHEUMATISM COUNCIL

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EDITORIAL

THE Editors regret that, owing to circumstances arising from the War, the publication of the Autumn number of the ANNALS has been delayed. For similar reasons the annual review of Recent Investigations into Rheumatism and Arthritis in America by Dr. Philip Hench, which has been a valuable feature hitherto, has had to be postponed; it is hoped to include it, together with other important papers, in the Spring 1943 number.

The Editorial Committee have noted with regret the death of Dr. Ludwig Aschoff of Freiburg-im-Breisgau, who contributed an important article to the first volume of the Annals and whose work on Rheumatism gained him a world-wide reputation.

The Editors will be glad to receive and consider articles bearing on the problems of the Rheumatic Diseases and, at the present time, would welcome especially reports from the Services. Twenty-five reprints will be supplied free of charge to contributors provided the order is given at the time of returning proofs. An estimate will be furnished on request if additional copies are required.

During the war, in view of the need for economy in paper, two issues only of the ANNALS OF THE RHEUMATIC DISEASES will be published annually instead of four. Subscribers' payments will be adjusted accordingly.

ANNALS
OF THE
RHEUMATIC DISEASES

METABOLISM, TOXICITY AND MANNER OF ACTION OF GOLD COMPOUNDS USED IN THE TREATMENT OF ARTHRITIS

III.—COMPLETE EXCRETION STUDIES AND COMPARISON OF INTRAVENOUS AND INTRAMUSCULAR ADMINISTRATION OF SOME GOLD SALTS

By R. H. FREYBERG, WALTER D. BLOCK and S. LEVEY
From the Rackham Arthritis Research Unit, the Medical School, University of Michigan, Ann Arbor*

Our investigations of the metabolism of gold were begun several years ago in an attempt to solve some of the mysteries concerned with the manner of action and toxicity of various gold salts employed in the treatment of arthritis. It seemed reasonable that, if more complete information were available regarding the fate of gold administered to humans in different ways, the relative value of different types of gold preparations could be more scientifically ascertained and improved methods of administration of such drugs would result.

To accomplish these studies, special methods of quantitative gold analysis were developed. However, successful analysis of the gold content of fæces was not possible until considerable information had been obtained regarding the plasma and synovial fluid concentrations of gold and the urinary excretion of gold. Consequently, these results were reported separately as they were observed following the treatment of patients with rheumatoid arthritis with gold sodium thiomalate (myochrysine), gold sodium thiosulphate, and colloidal gold sulphide. Much valuable information resulted from these earlier studies. However, they did not include fæcal gold analyses, and whenever administered parenterally the salts were injected intramuscularly. When the

* The Rackham Arthritis Research Unit is supported by the Horace H. Rackham School of Graduate Studies of the University of Michigan.

technical advances permitted, we studied more patients in a similar fashion, but made complete excretion studies, including the fæcal gold elimination. Comparison was also made of the intramuscular and intravenous routes of administration of some gold salts. It is the purpose of this communication to report the results of these extended studies.

Methods

Patients with rheumatoid arthritis were studied, using a plan of investigation and technical procedures precisely the same as employed in our earlier investigations.[1] Fæcal gold was determined by the method of Block and Buchanan.[2, 3] Usually analyses of daily accumulated fæces were made; occasionally two or three days' eliminations were pooled, analysed and reported as average daily excretions.

Results

In Fig. 1 are the results obtained in subject A. B., which are characteristic of those of all patients to whom gold sodium thiomalate* was given intramuscularly. The plasma concentration and urinary excretion of gold were similar to those previously reported in other subjects treated with this salt. The fæces contained much less gold than did the urine. The fæcal excretion increased slightly as the amount of gold injected increased. There was some variation from day to day, and it is conspicuous that during the twenty-four-hour period following injections of gold salt the fæcal excretion was *not* greater than on other days; this distinctly contrasts with the urinary elimination of gold. During the seven days following the injection of 40 mg. of gold (on the eighteenth day) the urinary excretion of gold was only 7·5 mg., and the fæcal excretion only 2 mg. Thus only 24 per cent. of the injected gold was eliminated before another injection was given, following which there was still greater retention. From our earlier studies, when only urinary excretion was measured, it was evident that there was considerable retention of gold during the period when the gold salt was being administered; now with these complete excretion data, the exact amount of retention of gold is definitely known, and is found to be approximately 75 per cent. of the amount administered.

* Myochrysine, marketed by Merck and Company, Rahway, New Jersey.

Fig. 2 contains results obtained when gold sodium thiosulphate* was injected intramuscularly. In this particular patient blood concentrations were lower than commonly observed with this salt; the urine values are of the usual magnitude.[1] It should be observed that with this gold preparation also the amount of gold excreted in the fæces was much less than that in

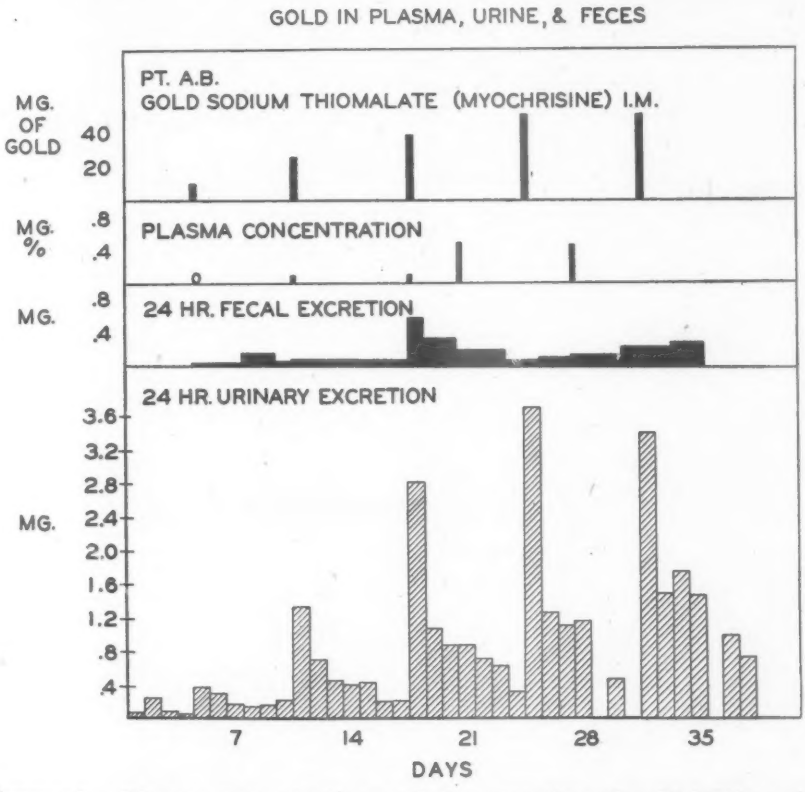

FIGURE 1.—Plasma concentration and the excretion of gold in the urine and fæces of a patient treated with gold sodium thiomalate (myochrysine) injected intramuscularly at weekly intervals. Increasing doses were employed until the dose contained 50 mgm. of gold.

the urine, and that the fæcal excretion increased as the amount injected increased, but it did not continue to rise after the weekly dose remained constant, even though the gold was being retained. The fæcal gold values are slightly higher in this patient than were found after injection of gold sodium thiomalate (Fig. 1). With the use of this salt also, during the period of administration, most of the gold injected is retained in the body. In general,

* Supplied for this study by G. D. Searle and Company, Chicago, Illinois.

the metabolism of gold is similar following intramuscular injections of gold sodium thiomalate and gold sodium thiosulphate.

Several patients were given gold sodium thiosulphate intravenously in order to contrast results with the intramuscular route of administration. In Fig. 3 the results of intravenous and intramuscular injections in the same patient are shown. During the period of increasing intravenous doses the plasma

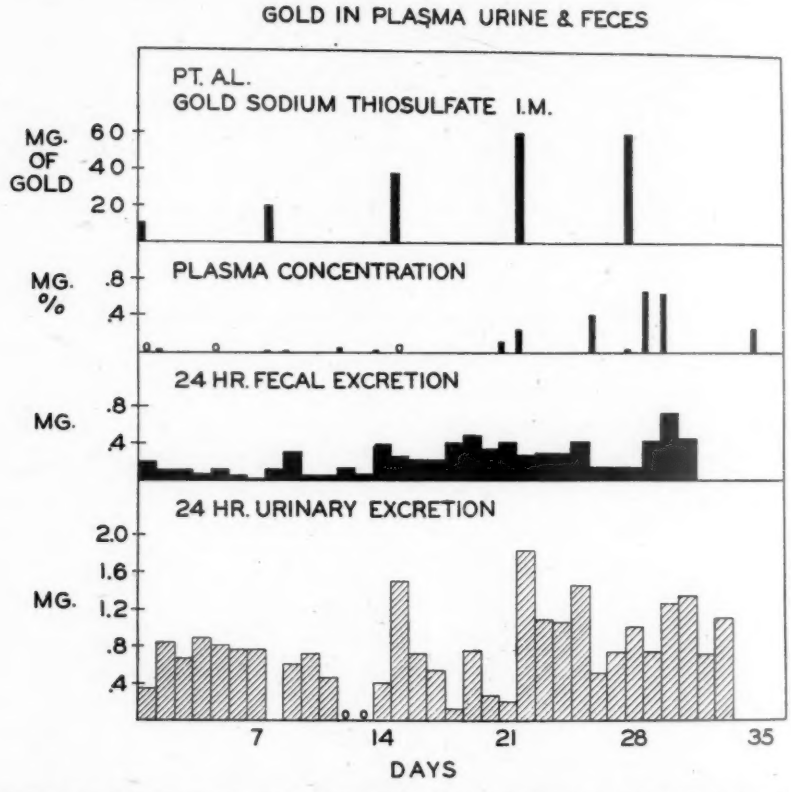

FIGURE 2.—Plasma concentration and the excretion of gold in the urine and fæces of a patient treated with gold sodium thiosulphate injected intramuscularly at weekly intervals. Increasing doses were employed until the dose contained 60 mgm. of gold.

concentration and the urinary excretion of gold were essentially the same as observed in other patients given the salt intramuscularly. Most significant is the fact that the plasma concentration and the urinary and fæcal excretion of gold were essentially the same when the same amount of the gold salt was injected, whether it was given intravenously or intramuscularly. In a week following the injection of 40 mg. of gold intravenously *and also intramuscularly* 24 per cent. was eliminated, 76 per cent.

retained. These values are identical with the results following injection of the same amount of gold as gold sodium thiomalate.

Another interesting finding in connection with the studies following intravenously injected gold sodium thiosulphate was that the blood concentration and urinary excretion during the first few hours after injection (Fig. 4) were similar to those following the intramuscular injection of this salt, reported previously.[1] This observation indicates the relatively quick

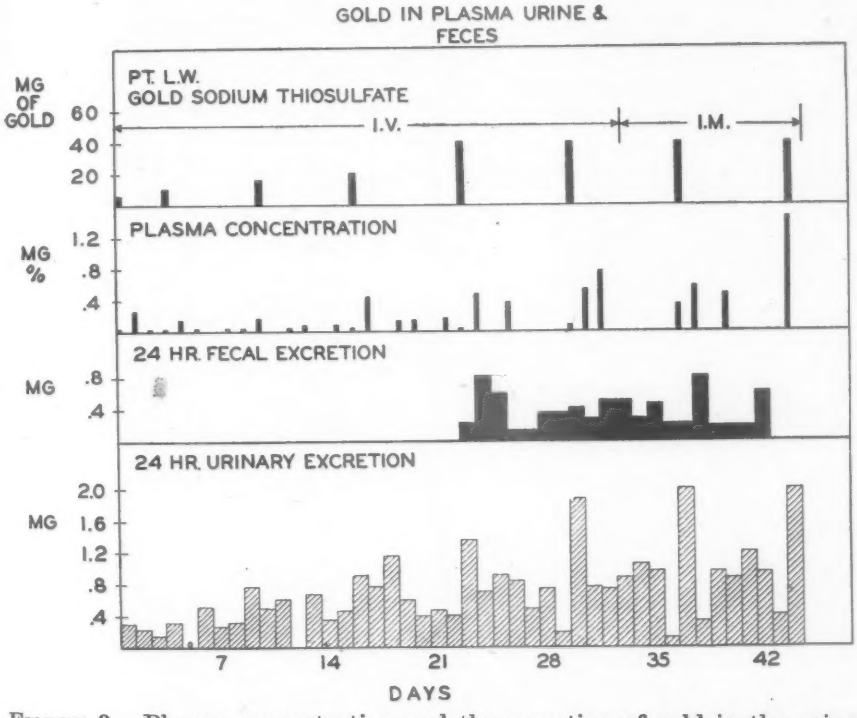

FIGURE 3.—Plasma concentration and the excretion of gold in the urine and fæces of a patient treated with gold sodium thiosulphate injected at weekly intervals at first intravenously, then intramuscularly. Increasing doses were employed until the dose contained 40 mgm. of gold, at which level it remained throughout the remainder of the study.

absorption of this soluble gold salt when it is given intramuscularly. One hour after the intravenous injection the plasma gold concentration was only slightly higher than observed two, three and four hours after injection, thus indicating the slow rate at which gold leaves the blood stream.

In earlier studies it was found that most patients given colloidal gold sulphide* orally or intramuscularly had very low

* *Aurol Sulphide*, supplied for this study by Hille Laboratories, Chicago, Illinois.

plasma gold concentrations, and eliminated little gold in the urine. The present investigations substantiate our earlier results, and further indicate that the fæcal excretion of gold following administration of this colloidal suspension is exceedingly small. Findings in a typical case appear in Fig. 5. After twelve intramuscular injections of colloidal gold sulphide, each containing 38 mg. of gold, the plasma contained only traces of gold, and after

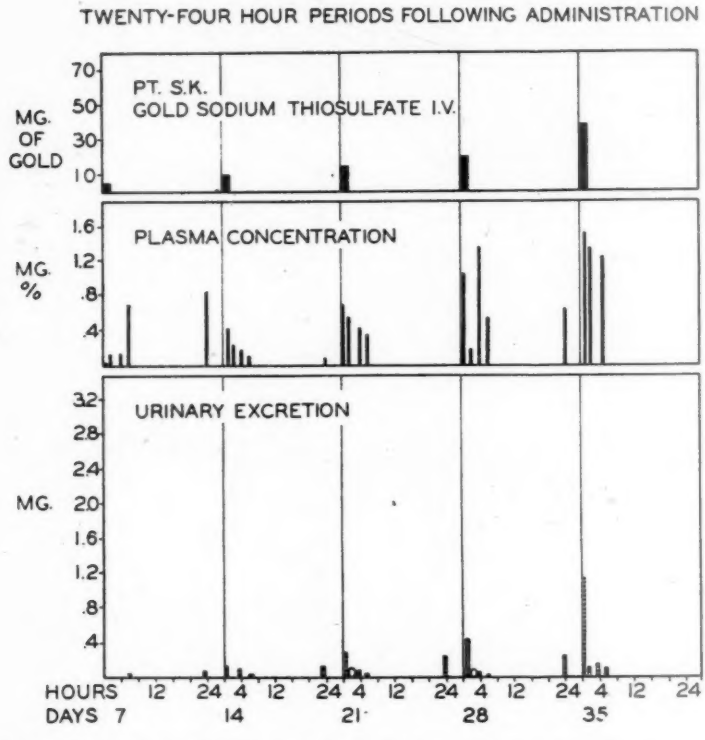

FIGURE 4.—Plasma gold content at one, two, four, six and twenty-four hours after the intravenous injection of gold sodium thiosulphate, and the gold content of the urine formed between the time of blood analyses. The injections are indicated by the vertical lines extending through the graph.

sixteen injections the fæcal gold values were very small. The urinary output of gold was measured for seven days; on four days no gold was found in the urine. Results in other patients were similar.

Most surprising results were obtained after *intravenous* injections of colloidal gold sulphide. The data in Fig. 6 show that after a single large injection of colloidal gold sulphide containing 50 mg. of gold the plasma contained little or no gold during the

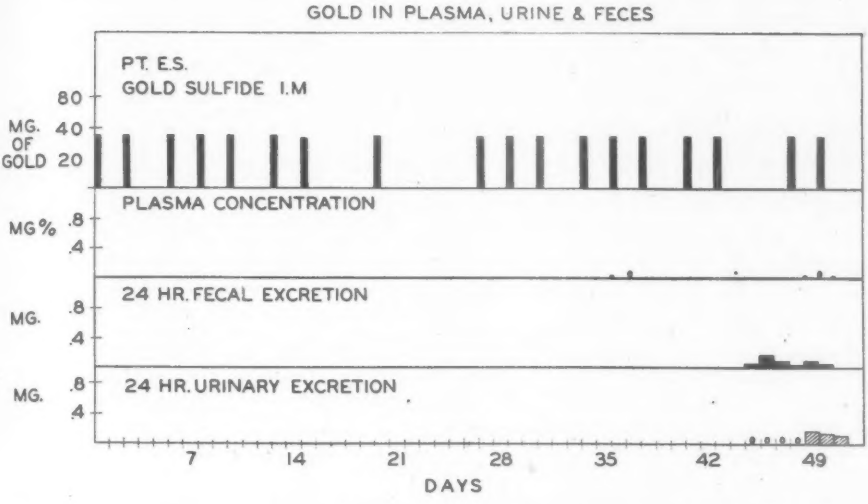

FIGURE 5.—Plasma concentration and the excretion of gold in the urine and fæces of a patient treated with colloidal gold sulphide injected intramuscularly in doses containing 38 mgm. of gold.

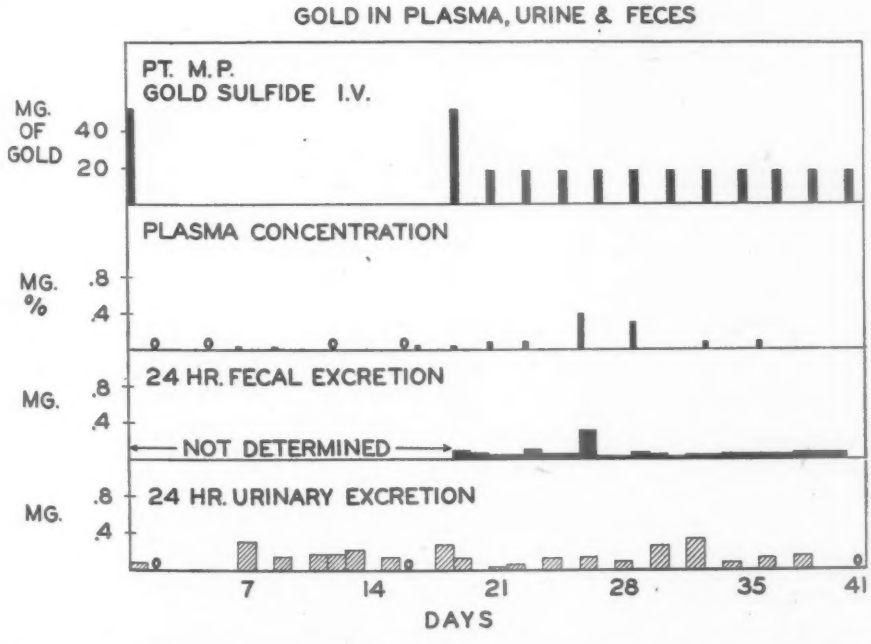

FIGURE 6.—Plasma concentration and the excretion of gold in the urine and fæces of a patient treated with colloidal gold sulphide injected intravenously.

following eighteen days; the excretion of gold in the urine was *much* less than occurred after the same amount of gold was injected as gold sodium thiomalate or gold sodium thiosulphate. When colloidal gold sulphide was injected intravenously in amounts supplying 20 mg. of gold every second day, the plasma concentration was slightly greater than after the single larger injection, but the excretion of gold in urine and fæces was small.

Another patient, S. A. (Fig. 7), was given large amounts of colloidal gold sulphide intravenously, the last injection containing

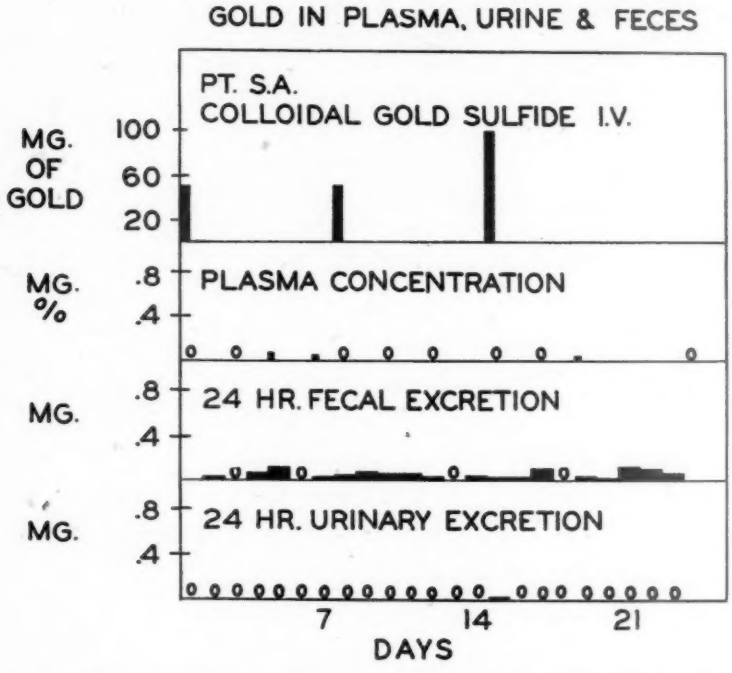

FIGURE 7.—Plasma concentration and the excretion of gold in the urine and fæces of another patient treated with colloidal gold sulphide injected at weekly intervals intravenously.

100 mg. of gold. Frequent morning samples of plasma contained either no gold or only traces; the urine contained no gold except a trace on two days, and the fæces contained very small amounts of gold. Specimens of plasma and urine obtained at short intervals after intravenous injection of colloidal gold sulphide were analysed (Table I). In subject S. A. the injected gold had disappeared entirely or was present only in traces as early as thirty minutes after injection; the urine contained no gold and the fæces only traces. Similar results were observed in M. P.

TABLE I.—THE PLASMA GOLD CONCENTRATION AND EXCRETION OF GOLD DURING THE TWENTY-FOUR HOURS AFTER THE INTRAVENOUS INJECTION OF COLLOIDAL GOLD SULPHIDE.

Date.	*Hour.*	*Gold Injected.*	*Plasma Gold Content.*	*Urine Gold Content.*	*24-Hour Fæcal Gold Content.*
	a.m.	Mgm.	Mgm.%	Mgm.	Mgm.
Patient S. A.:					
January 7	7.50		0	0	0
	8.00	50			
	8.05		1·22		
	8.10		0·03		
	8.15		0·33		
	8.30		0	0	
January 8	8.00			0	0·02
January 14	7.50		0	0	
	8.00	50			
	8.05		0·43		
	8.10		0·38		
	8.15		0·02		
	8.30		0·02	0	
January 15	8.00			0	0·03
January 21	7.50		0	0	
	8.00	100			
	8.05		16·50		
	8.10		1·19		
	8.15		0·48		
	8.30		0·15	0·01	
January 22	8.00			0	0·02
Patient M. P.:					
November 7	7.50		0	0	
	8.00	50			
	8.07		1·38		
	8.14		1·27		
	8.31		0·26		
	9.00		0·07	0·02	
	10.00		0·03	0	
November 8	8.00		0	0	
November 25 ..	7.50		0·02	0·27	
	8.00	50			
	8.09		1·66		
	8.16		0·61		
	8.31		0·28		
	9.00		0·05	0·01	
	10.00		0·05	0·02	
November 26 ..	8.00		0·05	0·05	0·09

Continuous excretion studies conducted in seven patients using gold sodium thiomalate, gold sodium thiosulphate, and colloidal gold sulphide are summarised in Table II. Results were similar with the first two salts; the gold of these salts was excreted chiefly in the urine and the retention ranged from 77 to 88 per cent. But in the case of colloidal gold sulphide more than 99 per cent. of the gold was retained and the excretion was chiefly in the fæces.

Discussion

It was evident from our earlier studies, when urinary excretion only was measured, that considerable retention of gold occurred during the period of its administration. From the present investigations, which include the determination of gold in fæces as well as in the urine, the retention was accurately measured and found to be great. During the many weeks when gold sodium thiomalate and gold sodium thiosulphate were injected the total excretion of gold was never more than 23 per cent.; usually it was between 10 and 15 per cent. of the amount injected. The retention of gold given as colloidal gold sulphide was usually greater than with the crystalline salts, regardless of the route of administration.

The chemical aspects of blood, urine and fæces obtained after the intravenous injection of gold sodium thiosulphate are essentially the same as when this salt is given intramuscularly, indicating that the absorption from muscle depots is rapid and that the metabolism of gold given as this salt is not appreciably affected by the route of administration. The finding of only 3·64 per cent. of the gold injected as gold sodium thiosulphate in the muscles of rats one day after injection,[4] is further evidence of the rapid absorption.

Even when injected directly into the blood stream, a large part of the gold is retained in body tissues for a long time. Details of this retention are being studied.[4, 5]

Since our metabolism data show close similarity between gold sodium thiomalate and gold sodium thiosulphate, it seems correct to conclude that the absorption of gold given intramuscularly as the thiomalate salt is rapid and quite complete. This conclusion is supported by the finding of only 7·6 per cent. of the gold injected into the muscles of white rats in the form of gold sodium thiomalate to be present at the site of injection one day later.

TABLE II.—EXCRETIONS COMPARED WITH THE INTAKE OF GOLD DURING TREATMENT WITH VARIOUS GOLD PREPARATIONS.

Patient.	*Preparation.*	*Route of Administration.*	*Number of Days Analysed.*	*Total Intake of Gold.*	*Excretion of Gold.*				*Retention of Gold.*
					In Urine.	*In Fæces.*	*Total.*		
				Mgm.	Mgm.	Mgm.	Mgm.	Per Cent. of Intake.	Per Cent.
A. B.	Gold sod. thiomalate (myochrysine)	Intramuscularly	39	173	27·8	5·1*	32·9	19·0	81·0
M. B.	Gold sod. thiomalate (myochrysine)	Intramuscularly	39	168	20·3	3·6†	23·9	14·1	85·9
A. L.	Gold sod. thiosulphate	Intramuscularly	39	168	18·3	6·6*	25·0	15·0	85·0
A. D.	Gold sod. thiosulphate	Intramuscularly	39	168	14·4	5·2†	19·6	11·7	88·3
C. D.	Gold sod. thiosulphate	Intramuscularly	39	128	21·6	7·8 –	29·4	23·0	77·0
E. S.	Colloidal gold sulphide	Intramuscularly	7‡	114	0·40	0·60*	1·0	0·9	99·1
S. A.	Colloidal gold sulphide	Intravenously	25	200	0·007	0·55*	0·6	0·3	99·7

* Analysed.
† Calculated on basis of analytical results in other patients.
‡ Analyses made on 45-51 days of treatment, while 38 mg. gold were injected three times a week.

From our earlier investigation we suspected the low plasma and urinary excretion values observed when colloidal gold sulphide was given orally or intramuscularly were due to poor absorption. However, the data of this report show rapid disappearance of gold from the blood *after the intravenous injection* of this colloidal preparation, and it is not excreted. Animal investigations have shown that reticulo-endothelial cells of the liver and spleen contain huge amounts of precipitated gold after this colloid gold sulphide was injected.[6] It seems clear, therefore, that the rapid disappearance of intravenously injected colloidal gold sulphide is due to phagocytosis by reticulo-endothelium. In this respect this colloidal gold salt behaves like other colloidal suspensions injected intravenously. Because of this, it seems obvious that colloidal preparations of gold or gold salts are not advantageous, nor are they to be recommended for treatment.

Summary and Conclusions

Further investigations of the metabolism of gold used in the treatment of rheumatoid arthritis, including complete excretion studies and a comparison of effects following the intravenous and intramuscular injections of some gold salts, are reported.

During the period of administration of gold sodium thiomalate and gold sodium thiosulphate the fæcal excretion of gold is much less than the urinary elimination, ranging from 12 to 25 per cent. of the total excretion. Following the injection of colloidal gold sulphide, the total excretion is much less than that found after the injection of the crystalline salts, but the percentage in fæces is considerably greater. These complete excretion studies show that gold is retained in *large* amounts during the period of treatment; the retention ranged from 77 to 88 per cent. with the crystalline salts, and often more than 99 per cent. with colloidal gold sulphide.

When gold sodium thiosulphate is used, the plasma content and excretion of gold are essentially the same whether the drug is given intravenously or intramuscularly. Therefore the factor of absorption from a muscle depot has no important influence on the metabolism of this crystalline gold salt, and probably also not on the metabolism of gold sodium thiomalate.

Within thirty minutes after an intravenous injection of a large amount of colloidal gold sulphide the plasma may contain little or no gold, and the amount excreted during this period is

very small or none. After many intravenous injections of this preparation the plasma gold concentration and excretion of gold are small and similar to the values usually observed following oral or intramuscular administration. These results are due to quick phagocytosis of the colloidal gold salt by reticulo-endothelial cells.

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RESISTANCE IN RHEUMATISM

By WILLIAM HUGHES

Current conception of the mechanism of a disease such as rheumatism postulates the existence of an infective agent which "acts on" or "attacks" the tissues and "produces" a lesion. Certain factors such as age, sex, the presence of septic foci, glandular dysfunction, etc., contribute by lowering the "resistance." In this vague concept all the terms in inverted commas are capable of more than one interpretation, but the one which has caused most confusion in the study of rheumatism is "resistance." This term has been stretched to accommodate the most contradictory hypotheses in the ætiology of the disease, and some promising methods of treatment have been emasculated

to conform to the hypothetical requirements of "resistance." It is used in immunology to describe part of the complicated dynamic reaction of the host to the infective agent. In the study of the comparatively simple inflammations of experimental pathology it has a circumscribed technical significance. Once it is translated into clinical medicine this definition is lost and confusion results. In Koch's phenomenon, for example, the intense inflammation and necrosis following the second injection of tubercle bacilli is regarded by the immunologist as a sign of high resistance, even though he knows the guinea-pig is suffering from a fatal disease and will certainly die in a short time. In man an injection of tuberculin is followed by a vigorous local reaction—a lesion of a kind—in a previously infected subject. But the reaction is considerably modified or may be completely repressed, as noted originally by von Pirquet (1911), (*a*) if the subject is very ill, (*b*) is suffering from some forms of intercurrent disease (*e.g.*, measles), or (*c*) is pregnant (Nobécourt and Paraf, 1920).

It seems hardly necessary to point out that in this particular instance the absence of the tuberculin reaction in the pregnant woman or debilitated subject is due to lowered resistance. But few clinicians can envisage the possibility of lowered resistance abolishing a lesion. When Hench (1933A) made the extremely interesting discovery that the lesion of rheumatism disappeared during pregnancy, the significance of the part played by lowered resistance in achieving this phenomenon passed unnoticed. So inflexible are the *a priori* demands of increased resistance that the most roundabout and far-fetched mechanisms were invented to account for the results on orthodox lines. Resistance to the clinician with his mind firmly fixed on the outcome of the disease is really a measure of his patient's capacity to survive. The severity of the disease depends on the magnitude of the lesion, and it is difficult to accept the possibility of a high resistance increasing the amount of lesion and, consequently, disease, and a low resistance diminishing the lesion and bringing about temporary or permanent cure.

Still (1897) recorded three cases of juvenile rheumatoid arthritis which showed remarkable improvement after measles, scarlet fever and catarrhal jaundice respectively. In 1903 Wishart reported four cases of chronic rheumatism whose symptoms disappeared with the onset of jaundice. Hench (1933B)

rediscovered this phenomenon of repression of rheumatic lesions by jaundice. Following Wishart's suggestion that the excess of circulating bile was the curative principle, Hench and other American physicians (Hench, 1938; Thompson and Wyatt, 1938; Sidel, 1938; Rawls, 1938) made an extensive investigation into the therapeutic possibilities of bile salts and pigments without success. The possibility that improvement might be due to the disease associated with jaundice rather than the jaundice itself was not explored. Here again certain immunological data have not been assimilated. Pearce (1928) has published a series of experiments showing the effect of implanting vaccinia virus and *Sp. pallida* simultaneously in the testicle of a rabbit. Briefly, the evolution of the syphilitic lesions was always delayed. In a controlled series the delay in appearance of the primary lesion amounted to 40·1 days. This is a long time in the life of a rabbit. Many such instances showing the effect one disease can have on the lesions of another have been recorded in clinical medicine; but here the suppression of lesions is usually referred to as temporary cure. Apart from the instance quoted above the best clinical illustrations are seen in leprosy, where the phenomenon is quite common. Muir (1927) considered that kala-azar could produce a real cure in certain stages of leprosy, and noted that many diseases including enteric fever, dysentery and malaria can produce temporary flattening out of the lesions. He notes (1934) that pregnancy and practically any form of debility will inhibit the leprolin reaction—the counterpart of the tuberculin reaction in tuberculous subjects. The effect of malaria on the lesions of general paralysis provides another good clinical example of this phenomenon.

In connection with jaundice some further significant observations were made by Hench (1938). He noted that the symptoms frequently cleared up in the pre-icteric stage; which shifts the emphasis from the bile pigments to the antecedent debility. The origin of the jaundice was immaterial. There was a "zone of therapeutic effectiveness"—that is, the more intense the jaundice the more likely were the lesions to recede. Atophan (cincophen) jaundice with a 46 per cent. mortality (Palmer and Woodall, 1936) was extremely effective, which, as we shall see, parallels the findings in gold therapy where "toxic cases" do best. Here, then, is a large body of clinical and immunological evidence going to show that the lesions of rheumatism and some

other diseases can be modified or repressed by agents which lower resistance.

A brief reference to the measures which immunologists have used to suppress the reaction of anaphylaxis will help to throw some further light on the mechanism by which certain drastic treatments bring about cure in rheumatism. We find the most diverse agents credited with the power of inhibiting the development of anaphylaxis. Hill and Martin (1932), in a valuable review of the subject, give a long list of agents which have been reported as effective in inhibiting the reaction. Included in the list we find such diverse agents as milk, peptone, colloids, dyes, surgical operations, vitamin deficiency, starvation, pregnancy and intercurrent disease, etc. There is more than a superficial resemblance between these agents and the agents which, as we shall see later, have been described as little short of miraculous in the treatment of rheumatism. It would be just to conclude that practically any material interference will inhibit the development of a fatal reaction in anaphylaxis. Hill and Martin observe that even sodium chloride, if the dose is "pushed," will inhibit the reaction, but they point out that sickness and death frequently result from the therapeusis. It is difficult to express all that is implied by such an observation. It means that to initiate this reaction which may entail injury to tissues, or even its own death, the body must be in a reasonably good state of health and free from undue material interference when the exciting stimulus is applied. This presents no difficulty to immunologists, who regard the anaphylactic reaction as a manifestation of high resistance and are prepared to see it inhibited by agents which lower the resistance. The clinician finds it difficult to assimilate such a conclusion in his conception of the mechanism and treatment of rheumatism. Using similar or identical agents in the treatment of rheumatism, he has been at infinite pains to show—often by verbal subterfuge—how they increase rather than diminish the resistance and so bring about cure.

Generally speaking, measures which increase the resistance—sanatorium regime, eradication of small septic foci—have not been followed by rapid or spectacular success in rheumatism. It has been said that the path of therapeutics in this disease is strewn with the ghosts of rational treatments—the latter always based on efforts to increase resistance. At the same time, intuition, accident and empirical observation have introduced us

to many agents which have brought about spectacular cures. A selection from the literature is set out on p. 94 in a classification intended to bring out the relation between the debility associated with each agent and its curative effect.

A few words of comment on the reliability of the data for the classification are necessary. The observations on the effects of pregnancy and jaundice and infectious disease can be accepted without difficulty, chiefly because they are made without the prejudice that goes with the introduction of a new form of treatment. With regard to the various forms of treatment one should make allowance in each case for prejudice on the part of the author. I have, therefore, given authority for every treatment which is not adequately described in the average textbook.

It will be seen from the classification that the more toxic or debilitating the agent the better is the result. Commenting on the effects of jaundice, Hench noted that it brought about remission of symptoms with more rapidity and certainty than any other physiological change or pharmacological agent known. Hench (1933) first noted this repression of rheumatic lesions in cases of jaundice due to atophan poisoning.

Lagèze (1939), reporting a fatal case of stomatitis and jaundice following gold therapy, found that the rheumatism cleared up before death. Hartfall and Garland (1935) in their original series of cases treated with gold had a 3 per cent. mortality. Ellman and Lawrence (1938) report favourably on gold therapy. They had one death from agranulocytosis besides the usual series of toxic reactions in a series of 16 cases. Phillips (1936), one of the few Americans to try gold, had to give it up on account of the number of toxic reactions. He confesses he did not feel competent to handle the drug to the advantage of the patient. Incidentally, it is constantly reported in the literature that "toxic" cases in gold do very well (Crosby, 1936; Tegner, 1937).

We should expect that any drug given in excessive doses would produce good results in a percentage of cases. In leprosy ½ ounce of potassium iodide daily will repress the lesions; in anaphylaxis excessive dosage of sodium chloride will prevent the reaction if the animal survives. It is interesting to note that this type of therapy is represented in rheumatism by giving excessive doses of vitamin D—probably the only vitamin which lends itself to such a purpose. Dreyer and Reed (1936) had to

CLASSIFICATION

Agent.	*Authority.*	*Therapeutic Effect.*
1. *Trauma :*		
(*a*) *Severe :*		
(i) Fractured femur ..	MacKenzie (1931)	Excellent
(ii) Major operations:		
Parathyroidectomy ..	Leriche (1931, 1933)	Often spectacular
Unsuccessful parathyroidectomy	Schkurov (1935)	Good
"Mock" parathyroidectomy	Simon & Weill (1932)	Very good
Symp. ganglionectomy ..	Young (1936)	Very good
	Learmonth (1937)	Fair
(*b*) *Mild :*		
(i) "Bone forage" ..	MacKenzie (1936)	Fair
	Kersley (1938)	Fair
(ii) Minor operations:		
Tonsillectomy, dental extractions	Hench *et al.**	Poor
(*c*) *Minor injuries and irritations :*		
Massage, manipulations, autohæmotherapy, baths, colonic lavage, etc.	Hench *et al.**	Uncertain, poor
2. *Concurrent Disease :*		
Measles, scarlatina	Still (1897)	Very good
Jaundice	Still (1897)	Very good
	Wishart (1903)	Very good
	Hench (1933B)	Good
Malaria	Cecil *et al.* (1935)	Good initial results, not sustained
3. *Metabolic Agents :*		
Pregnancy	Hench (1933B)	Very good
Starvation	Pemberton (1942)*	Good
Pernicious anæmia at "lemon yellow" stage	Hench (1938)	Very good; relapse when anæmia cured
Insulin (normal dosage) ..	Short & Bauer (1935)	General condition improved; arthritis worse
4. *Drugs :*		
(i) Atophan (Cincophen):		
Toxic cases:		
Jaundice, severe	Hench (1938)	Very good
Jaundice, light	Hench (1938)	Uncertain
Urticaria, severe	Rawls (1938)	Very good
Urticaria, slight	Rawls (1938)	No effect
(ii) Gold:		
Toxic cases:		
Jaundice, exf. dermatitis, stomatitis	Lagèze (1939),	Very good
	Crosby (1936),	Very good
	Tegner (1937)	Good
(iii) Vitamin D:		
200,000–1,000,000 units ..	Dreyer & Reed (1936)	Good
Normal dosage	—	(?) No effect

CLASSIFICATION—*Continued*

Agent.	*Authority.*	*Therapeutic Effect.*
5. *Biological Agents :*		
(i) Diathermy fever	Short & Bauer (1935)	Good initial results, not sustained
(ii) Intravenous vaccines:		
(*a*) T.A.B.	Hench (1941)*	Fair
(*b*) Streptococcal ..	Wetherby (1941)	Good
(iii) Subcutaneous vaccines ..	—	Useless

* Every year Hench and his colleagues publish a lengthy and informative review of chronic rheumatic diseases. The most recent is the *Seventh Rheumatism Review* (Hench, Bauer, Dawson, Hall, Holbrook, Key, McEwen, 1941). Mention is made of all the agents described in one or other of these reviews.

give up to 1,000,000 units daily to achieve results. This is five times the maximum safe dose according to Park (1938).

There is a gradual decline in therapeutic effect as the toxicity of the agent decreases. Atophan jaundice with a 46 per cent. mortality ranks high as a therapeutic agent; raising the resistance by means of sanatorium regime gives poor results.

The effects of trauma on the rheumatic lesion show a similar trend. The severe trauma of a fractured femur was so effective that it inspired MacKenzie to develop what has now become known as " bone forage " (MacKenzie, 1936; Kersley, 1938). In this operation a piece of bone is drilled away. Possibly with refinement of technique the trauma has been attenuated and successes are not now reported so often in the literature.

Leriche (1931, 1933) postulated a disordered calcium metabolism in rheumatism, and by surgical assaults on the affected bone, parathyroids and local sympathetic ganglia, achieved results which he described in some cases as miraculous, but he confesses that they were not permanent. The rational basis of his success was exploded by Simon and Weill (1932) when they found a " mock " operation on the parathyroid did just as well. Again, Schkurov (1935), who had good results from operation on the parathyroid in 83 cases, had tissues sectioned after removal at operation. In 23 cases no parathyroid was found. Further, it appears that in cases where ganglionectomy is performed (Young, 1936; Learmonth, 1937) the improvement is not confined to the joints supplied by the ganglia which were removed.

As we descend from these major traumata to minor operations on septic foci in the tonsils, sinuses, and teeth sockets, there is a decline in the percentage of successes.

I have classified massage under the heading of trauma. Many of the manipulations and vigorous forms of massage probably depend for their effect on a certain amount of tissue destruction. Wright (1938) has drawn attention to this possibility.

The results with artificial fever, however induced, may be spectacular at the beginning but are rarely permanent. Short and Bauer (1935), using diathermy, treated 25 cases. It is interesting to note that one of the 5 cases showing sustained improvement was that of a woman who became pregnant during the period of amelioration. Presenting a neat contrast with this is the case reported of a man who put on 9 lbs. in weight under the influence of insulin administration. At the end of ten months his general condition was excellent but his arthritis was much worse.

Pemberton (1942) mentions that cures have followed starvation diets of the "Hollywood" type, although he does not approve of them. He considers that there is alimentary dysfunction in rheumatism which should be treated by withholding fat. Giving a high protein and carbohydrate, low-calorie diet, he claims to be able to increase the resistance and bring about improvement.

The classification emphasises the relationship between major debility and high therapeutic efficiency. Atophan, gold and excessive vitamin D have all been condemned as dangerous remedies and lauded for their beneficial effects. It is impossible to escape from the conclusion that a certain amount of debility is necessary if we are going to achieve results. There is plenty of scope, however, for ingenuity in devising safe measures to lower the resistance below the level at which lesions can occur. Trauma locally applied, for example, may have interesting possibilities. Osteotomy (bone forage) seems to have produced fair results. Massage and various forms of local interference continue to be used in treatment. In this respect it is interesting to note that as long as Pearce injected vaccinia virus and *T. pallidum* simultaneously into the same testicle the syphilitic lesions were repressed. When the vaccinia was inoculated at a distant site no such effect ensued. Similarly, when Ledingham

(1927) injected Indian ink and vaccinia virus into the skin of a rabbit no lesion occurred. A previous streptococcal infection had the same effect. But if the virus seeped out beyond the limits of the prepared area vesicles occurred. Possibly the same amount of trauma inflicted locally would be more efficacious than when applied at a distance in rheumatism. Refinement of technique must aim at reducing the mortality while retaining the trauma.

The following is an example of a method of treating gonococcal rheumatism evolved to meet an emergency. In Nigeria in pre-sulphonamide days gonococcal rheumatism was extremely common and difficult to cure. To treat the patient at rest for long periods constituted a special problem in hospital administration which disappeared after the introduction of sulphapyridine. Towards the end of 1941, however, our stocks of this drug became very low, and we had to conserve supplies for cases of pneumonia. In these circumstances I used a method of treatment introduced by Bryant and Fairman (1939) in the Sudan during an epidemic of cerebrospinal meningitis. They injected intramuscularly a saline suspension of M. & B. 693 tablets. We injected 10 c.c. of the suspension containing 1 gramme sulphapyridine into the buttocks. This is followed by fever and a large, diffuse and somewhat painful swelling of the buttock with almost simultaneous analgesia in the affected joints. In 14 cases treated the results were excellent and in 1 case spectacular. This was a policeman who had been treated by small and irregular doses by mouth for six weeks. Both wrist and knee joints were swollen and painful, and muscular atrophy was already obvious. He was sent up for invaliding. After three injections on alternate days the swellings had disappeared. The patient was discharged after ten days in hospital, and was back on duty within three weeks. Used in this fashion we were able to get as much effect with 3 or 4 grammes of sulphapyridine as might be expected from 20 to 50 grammes orally. Sulphapyridine is generally so effective by mouth that this is not a treatment which I particularly recommend, except in such circumstances as have been described. It is quoted merely to illustrate the therapeutic possibilities of attacking the lesion as well as the infection.

Discussion

The orthodox teaching in regard to resistance is based largely on Metchnikoff's theory in which pride of place is given to the cellular exudate in restraining infection. In simple experimental lesions it seems obvious enough that these cells exercise a useful function by phagocytosing organisms. The more cells there are in such a lesion the higher the resistance to infection; but, clinically, the bigger the lesion, the more severe the disease. In the complicated circumstances of disease, therefore, there is no simple solution to the problem of the various exudates, the space they occupy and the function they serve. Less and less reliance is being placed on the lesion as a barrier against the spread of infection. After much work on the subject Rich (1937) and his colleagues have been led to the conclusion that the lesion in tuberculosis, while it may have been designed for a useful purpose, never fulfils such a purpose in the actual circumstances of disease. Consequently they have tried to get rid of it by desensitisation. Clinically, the treatment of general paralysis by shock therapy provides the most successful example of lowering resistance in order to get rid of the lesion. Here the fate of the infection is ignored.

Unfortunately, the clinical ideal of immunity without lesions cannot always be realised. In leprosy, as in rheumatism and anaphylaxis, a recession of lesions can be achieved by practically any form of debility. But it would seem that the lesion in leprosy has some restraining influence on the infection because the disease usually recurs in a more widespread form after a drastic remedy has ceased to operate. The wave of bitter disappointment following the failure of each spectacular "cure" provides a warning against the facile assumption that resistance can always be lowered with impunity.

But if lowering resistance as a method of treatment has its failures in practice it does not necessarily follow that raising resistance is always safe. Some years ago an anti-streptococcal serum was introduced for the treatment of puerperal sepsis. In spite of—or, should we say, because of—the fact that it was a potent serum, it doubled the mortality of the cases treated (Colebrook, 1935). Convalescent (immune) serum has had an extensive trial in the treatment of poliomyelitis. Where controls were established results suggest that the serum is certainly

useless and probably harmful (Faber, 1941). In Roshenholtz' (1938) review there is one adequately controlled series which suggests that convalescent serum quadruples the mortality in this disease. The treatment of the same disease provides an interesting example of the effects of vigorous interference with the course of the disease. Orthodox treatment enjoins rest and often splints in the early stage and with remedial exercises later. Sister Kenny, who has established a world-wide reputation for her methods of treating this disease, advocates movements from the very first day. This is not the place to enter into the controversy about the value of the Kenny treatment, but it can be said that the treatment has stood up well to criticism and, on balance, it appears a little superior to that based on rest and increased resistance. Altogether it appears in this disease that measures directed towards increasing the resistance—immune serum and rest—are a little inferior to those which might reasonably be held to lower the resistance.

There is a sound rational basis for augmentation of resistance before infection is introduced. In the urgent circumstances of established disease, however, measures designed to increase the resistance—of which the lesion itself is an expression—are open to grave objections. Theoretically, it is not really surprising that such measures have had so little success. The main purpose of this article is to show that the use of trauma or debility to lower the resistance in rheumatism is a rational procedure. This hypothesis explains the empirical successes of the most diverse and often fantastic agents in rheumatism. There is one factor common to all successful remedies—we can describe it as shock, or trauma, or debility. Refinement of technique must be directed not so much towards attenuating the shock as to the discovery of the minimum amount of debility necessary for repression of the lesion.

It might be considered a disadvantage that the infective agent has not yet been identified in this disease. But whatever it is there is as yet no evidence that it propagates when the lesions are repressed. So long as there is no mortality associated with such measures we can apply them for the purpose of study with a good conscience, which after all is not the case in leprosy or general paralysis. Indeed, one could almost hope that the rheumatic infection would propagate during debility as this might lead to its early identification.

SUMMARY

The lesion in rheumatism is an expression of high resistance. It is a complicated and dynamic affair which can be simultaneously the source of disease and the basis of cellular resistance. It can be repressed by various debilitating agents—trauma, concurrent disease, disturbance of metabolism, dangerous drugs. In such circumstances there is no evidence that the infective agent, whatever it may be, propagates during the time the lesion is in abeyance.

Although the lesion is purposeful we cannot say that in rheumatism it fulfils any useful function. It is suggested, therefore, that in treatment we can ignore the infection, regard the lesion as physiologically unnecessary, and consciously adopt measures to lower the resistance.

The exploitation of this hypothesis should open up new and profitable fields of research in therapeutics.

A practical application in gonococcal rheumatism has been described.

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CULTURAL STUDIES ON RHEUMATOID ARTHRITIS AND RHEUMATIC FEVER

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THE literature on cultural studies in rheumatoid arthritis and rheumatic fever is so familiar to those interested in these diseases that no detailed description will be given; however, a few studies will be mentioned.

Cecil, Nicholls, and Stainsby[1] recovered streptococci from the blood and joints of the majority of their patients with rheumatoid arthritis, and Gray and Gowen[2] confirmed their observations. Dawson, Olmstead and Boots[3] were unable to do so. McEwen, Bunim and Alexander[4] recovered streptococci from the blood of 21 per cent. of their patients with atrophic arthritis and from 6 per cent. of the controls. Margolis and Dorsey[5] recovered streptococci from the blood and tissues from some of their cases and attached significance to the presence of these bacteria. Collins[6] obtained negative cultures from the synovial fluid of a large number of cases of atrophic arthritis. Blair and Hallman[7] were unable to isolate any significant organism from the synovial fluid or tissue of similar cases. Sabin[8], Findlay, Mackenzie and

MacCollum[9], and Preston[10] have all recorded negative results in their search for pleuropneumonia-like organisms in this disease.

The bacteriologic studies of rheumatic fever are just about as confusing and unsatisfactory. Cecil, Nicholls and Stainsby[11] and Clawson[12] have recovered streptococci in a high percentage of cases. Callow[13] has recovered streptococci of different kinds from a large number of cases; however, similar results were obtained on controls. McEwen, Alexander and Bunim[4] found streptococci in 17 per cent. of their cases, but the incidence was no more frequent than in controls. Green[14] also reported on the recovery of hæmolytic streptococci from the heart valves of patients dead with rheumatic fever.

It is evident that most workers have placed more emphasis on one of these diseases and have concentrated their efforts on either the blood or synovial fluid.

In 1936 we started to culture all available clinical and post-mortem material from suitable cases of rheumatoid arthritis and rheumatic fever. This study was continued over a period of four years. The studies were made on blood, synovial fluid, tissue and subcutaneous nodules from patients with rheumatoid arthritis, and on pleural or pericardial fluid, pericardial tissue or heart valves from cases of rheumatic fever.

In addition to cultural studies, most of the material was inoculated into mice by various routes and on to the chorio-allantoic membrane of chick embryos. The chick membrane and cultural methods for the detection of pleuropneumonia-like organisms are entirely adequate for the growth of most micro-organisms so that observations made by these special techniques considerably enhance the value of these studies. Tissues and fluids from several cases were also concentrated in an air-driven high-speed centrifuge for one hour at 29,000 r.p.m., and cultures of the sediment made.

Rheumatoid Arthritis

The patients selected for this study included only those in the active stage of the disease; that is, with pain and swelling of the joints and usually an increase in the sedimentation rate. No case was included if there was any doubt concerning the diagnosis.

The blood cultures were taken whenever possible in a dust-free, air-filtered room. Masks were worn by the operators during all procedures, and the transfers of cultures were made with rubber

bulbs on the pipettes. The aerobic clot method was used for most cultures. The principal medium used was dextrose phosphate broth. Repeated subcultures were made at intervals of five days for one month.

Forty-nine of 61 (80 per cent.) blood cultures made from 58 patients yielded no growth (Table I). The following organisms were obtained from 12 of the cultures: 5 yielded a large Gram-positive diplococcus (unclassified), 4 a *Staphylococcus albus*, 1 an alpha prime streptococcus, 1 a *Staphylococcus aureus*, and 1 a *B. subtilis*.

TABLE I.—BLOOD CULTURES ON PATIENTS WITH RHEUMATOID ARTHRITIS

No. of Patients.	*No. of Cultures.*	*Sterile.*	
		No.	*Per cent.*
58	61	49	80

Organisms Isolated	
Gram-positive diplococcus (unclassified)	5
Staphylococcus albus	4
Staphylococcus aureus	1
Alpha prime streptococcus	1
Bacillus subtilis	1
Total	12

Additional cultures were made of synovial fluid and tissue, as well as subcutaneous nodules on similar media enriched with horse blood (Table II). Twenty-four cultures of synovial fluid from 20 patients were sterile. Seven of 9 cultures of synovial tissue were sterile; a *Micrococcus tetragenes* was grown in 1 instance and a *Staphylococcus albus* in 1. Five of 9 subcutaneous nodules were sterile, 3 yielded a *Staphylococcus albus* and 1 a Gram-positive diplococcus.

TABLE II.—CULTURES OF JOINTS AND SUBCUTANEOUS NODULES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

Material.	*No. of Specimens.*	*Results.*	
		No Growth.	*Growth.*
Synovial fluid	24	24	0
Synovial tissue	9	7	2
Subcutaneous nodules	9	5	4

	Organisms Isolated	
TISSUE:	*Staphylococcus albus*	1
	Micrococcus tetragenes	1
NODULES:	*Staphylococcus albus*	3
	Gram-positive diplococcus	1

Special cultural studies were made according to the method of Klieneberger for the presence of a pleuropneumonia-like organism in the synovial fluid, synovial tissue or subcutaneous nodules from fifteen patients with rheumatoid arthritis (Table III). In no instance was such an organism recovered.

TABLE III.—CULTURAL STUDIES FOR PLEUROPNEUMONIA-LIKE ORGANISMS

Material Cultured.	*No. of Specimens.*	*Pleuropneumonia-like Organisms.*
RHEUMATOID ARTHRITIS:		
Synovial fluid and tissue	14	0
Subcutaneous nodules	5	0
RHEUMATIC FEVER:		
Synovial fluid	6	0
Pleural fluid	5	0
Pharyngeal washings	4	0
Heart	6	0
Lung	2	0

The synovial fluid, tissue or subcutaneous nodules from sixteen patients were inoculated on to the chorio-allantoic membrane of the chick embryo (Table IV); 141 eggs were inoculated and thirty subpassages made. No significant transmissible lesion was produced. The following organisms were isolated, one from each of three different cases: a *gamma streptococcus*, *Staphylococcus aureus* and *Staphylococcus albus*.

TABLE IV.—STUDIES ON CHORIO-ALLANTOIC MEMBRANE

	No. of Specimens.	*No. of Eggs.*	*No. of Passages.*	*Results.*	
				No Growth.	*Growth.*
RHEUMATOID ARTHRITIS:					
Synovial fluid and tissue	11	98	23	11	0
Subcutaneous nodules	5	43	7	2	3
RHEUMATIC FEVER:					
Synovial fluid	4	93	21	3	1
Pleural fluid	1	18	5	0	1
Heart	3	28	6	3	0

Organisms Isolated

RHEUMATOID ARTHRITIS:

Gamma streptococcus	1
Staphylococcus aureus	1
Staphylococcus albus	1

RHEUMATIC FEVER:

Alpha prime streptococcus	1
Staphylococcus albus	1

Similar material from seventeen cases of rheumatoid arthritis (Table V) was also instilled into the nares of 12- to 21-day-old white mice (Strain CF1) under light ether anæsthesia. Occasionally small areas of pneumonia developed after the first instillation. Thirteen of 127 mice injected in this manner developed small, patchy areas of pneumonia following the first instillation. Several passages (usually six) of normal and pneumonic lungs were made at intervals of from four to six days. In a few instances, a transmissible pneumonia developed; however, this was so irregular and inconsistent we feel that it was probably caused by a mouse virus or pleuropneumonia-like organism. Material from seven cases of rheumatoid arthritis was injected intravenously, intracerebrally, intraperitoneally, or subcutaneously into mice. No significant lesions were produced, nor was any transmissible agent recovered. Irradiated mice were used in many instances; however, no difference was found between these and the non-irradiated mice.

TABLE V.—RESULTS OF INTRAPULMONARY INOCULATIONS OF MICE.

	No. of Cases.	*No. of Mice.*	*No. of Passages.*	*Pneumonia after First Instillation.*
Rheumatoid arthritis ..	17	279	37	127/13
Rheumatic fever	16	486	85	145/14
Other diseases	32	183	19	116/16

RHEUMATIC FEVER

Tissues or exudates from 11 clinical cases and 10 autopsies with rheumatic fever were studied.

The following were cultured for pleuropneumonia-like organisms: synovial fluid (4), pleural exudate (3), pharyngeal washings (4), and heart valves with verrucous vegetations, pericardium or myocardium from five hearts obtained at autopsy (Table IV). Similar material from 11 of the cases which had been preserved by freezing was also cultured. In no instance were pleuropneumonia-like organisms recovered.

The pleural fluid from one and the synovial fluid from four clinical cases, as well as tissue from three hearts obtained at autopsy (Table IV), were inoculated on to the chorio-allantoic membrane and passed at intervals. No significant transmissible lesion was produced. An alpha prime streptococcus was obtained from one case and *Staphylococcus albus* from another.

Material from nine of the clinical cases and seven of the autopsies was instilled into the lungs of 145 mice and passages made as previously described (Table V). In all, 486 mice were used. Sixty-seven mice were inoculated by other routes with material from three of the clinical cases and six of the autopsies. The results of these studies were similar to those described above for rheumatoid arthritis.

Summary

Extensive cultural studies on special media, including the chorio-allantoic membrane, as well as the inoculation of mice, have been made on 85 cases of rheumatoid arthritis and 21 cases of rheumatic fever. No organism of significance has been consistently isolated.

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A REPORT ON A TEST OF MESTER'S "SPECIFIC" REACTION IN RHEUMATIC CASES

By W. S. C. COPEMAN and W. STEWART

The need is urgent for a specific test which will differentiate cases of true rheumatism, of any type, from those which should not be placed in this category. As Messoloff[1] wrote, "what we need is a specific reaction similar to the tuberculin test or the Wassermann reaction, which could be used as an absolute criterion in the diagnosis of all rheumatic manifestations. Until then all work done on this disease is prone to the many pitfalls and subject to the many difficulties that the students of tuberculosis and syphilis had to contend with less than a generation ago."

Mester[2] has recently claimed that he has found such a reaction, which depends upon the special sensitivity of rheumatic patients to salicylic acid.

His description of the test is as follows: The patients are resting and fasting. A count is made of the white blood cells, and after this count 1 c.c. of a 0·1 per cent. aqueous solution of salicylic acid is injected intradermally, forming five blebs of 0·2 c.c. each on the flexor aspect of the forearm, and after 30 minutes another white count is made. During this time the patient is forbidden to eat, drink, or make any effort. Nearly all rheumatic patients, acute, subacute or chronic, show after the injection a drop in the number of white cells after 30 minutes. The lowest figure regarded as positive was 15 per cent. below the level before injection, but diminutions as great as 50 to 70 per cent. were observed. The reaction appears to be positive in every kind of rheumatic infection—joints, heart, serous membranes, nerves, eyes, etc. In a series 98 per cent. of rheumatic cases gave a positive result, while all controls were negative.

Mester claimed that by the use of this test malingerers can be detected, and cases of arthritis which are not due to rheumatism —*e.g.*, tuberculous or syphilitic—can be divided off, since the test is positive only in cases of rheumatic fever, subacute rheumatism and chronic rheumatoid arthritis. He points out, however, that the results of the test must be read in conjunction with the clinical findings, as is the case with all biological tests.

Professor Lenoch[3] carried out this test in 140 cases, divided

into two groups, in the first of which a positive result was to be expected and in the second of which the number of leucocytes was not expected to be greatly changed.

The first group consisted of 43 cases of chronic rheumatic polyarthritis; 30 cases of secondary chronic polyarthritis; 2 convalescent from these diseases and free from symptoms; 3 cases of scapulo-humeral peri-arthritis; 5 cases of spondyl-arthritis ankylopoietica; and 5 cases of rheumatic (idiopathic) sciatica—a total of 88 cases. The second group consisted of 22 cases of spondyl-arthrosis deformans and osteo-arthrosis deformans, chiefly of the lower extremities; 1 case of static disturbances; 10 cases of gout; 2 cases of sequels of thrombo-phlebitis; 1 case of severe congenital dislocation of hip; 1 case of tuberculosis of the hip-joint; 6 cases of acute and subacute gonorrhœal polyarthritis; 1 case of sacralisation of the fifth lumbar vertebra; 3 cases of intermittent hydrarthrosis; 1 case of intermittent claudication from peripheral arterio-sclerosis; 1 case of chronic teno-synovitis of unknown origin; and 1 case of healed severe fracture of the pelvis.

Summing up the results of his investigation Lenoch stated that Mester's reaction is very often positive in rheumatic disease of the joints, and may even be positive in exceptional cases of diseases quite unconnected with rheumatism. " On the grounds of our experience in 140 cases, we regard this test as a probable addition to our methods of diagnosis of the so-called rheumatic diseases. Like most diagnostic aids this test is far from infallible, but it is of great value when it becomes necessary to decide whether an inflammatory condition of the joints is of rheumatic or other origin." He points out that it is negative, as claimed by Mester, in cases of degenerative arthritis (osteo-arthrosis). He ends with a warning against making a diagnosis of " rheumatic joint pains " or " myalgia " with the aid of this test.

Our own test was conducted on a series of 50 cases which were grouped as follows:

I. Rheumatic cases:
   (*a*) Acute and subacute rheumatism, 13.
   (*b*) Fibrositis, 5.
   (*c*) Sciatica, 4.
   (*d*) Rheumatoid arthritis, 1.

II. Osteo-arthritis, 1.

III. Meningococcal septicæmia (simulating acute rheumatism), 5.
IV. Acute tonsillitis, 1.
V. Subacute osteo-myelitis, 1.
VI. Control cases:
(*a*) Enuresis, 4.
(*b*) Gastric investigation cases, 13.
(*c*) The writers, 2.

All the cases were such as are admitted to the wards of a service hospital. The cases of acute and subacute rheumatism showed manifestations of active rheumatic disease. The results obtained are shown in Table I. The sedimentation rate is increased considerably.

A short summary of a few of these cases is given.

CASE 20.—Male, age 26, a member of an infantry regiment with 17 months' service. Illness had started with pain and swelling of left knee; admitted to bed in a reception station; while there tonsillitis set in followed by quinsy; had a similar attack the previous winter, and he had suffered from frequent sore throats. On admission there was involvement of both knees. His temperature was 101 and pulse 80.

CASE 21.—Male, age 38, with 5 weeks' service. Illness started with severe pain in hips and shoulders after a few days' initial drill; this was followed by bronchitis, requiring confinement to bed. After 8 days in sick-bay pain and swelling set in in left knee and he was unable to move the joint. Repeated attacks of tonsillitis occurred in the past. On admission there was gross swelling of left knee with marked restriction of movements. The temperature was 101 and the pulse 100. There was myocardial involvement. He had been an athlete (mile runner), and there was a strong family history of rheumatic disease.

CASE 28.—Male, age 38, with 7 months' service; a labourer in civil life. Illness started 12 days before admission with severe pain in the ankles and feet. He was unable to get about. Eight days later left wrist became involved. On admission temperature was 101 and pulse 100; both ankles and left wrist were much involved. Since 1934 he had had three attacks of acute rheumatism which seemed to have cleared up completely.

CASE 44.—Male, age 20, with 1 month's service. Admitted with pain and swelling of both knees, the left being slightly greater than the right. He had had 14 days' confinement to bed in a reception station, during which time there had also been swelling of right wrist, but this had gone down with complete recovery after a few days. The temperature after he arrived in the ward was 102 and the pulse 70.

CASE 18, which showed the greatest fall (−25·7 per cent.), was a male, age 36, with 4 days' service prior to illness. This illness started 16 days previously with a severe sore throat, severe pains in back and head, cold sweats and transient fainting attacks. The following day a rash appeared, at which time he was admitted to hospital. The rash was of scarlatiniform

TABLE I.—CASES OF RHEUMATISM, ACUTE AND SUBACUTE

Case No.	Total White Cells per c.mm.		Decrease or Increase per Cent. per c.cm.	Polymorphs per Cent.		Decrease or Increase per Cent. per c.mm.	Lymphocytes per Cent.		Decrease or Increase per Cent. per c.mm.	Monocytes per Cent.		Decrease or Increase per Cent. per c.mm.	Sedimentation Rate, 1st Hour.
	Before.	After.		Before.	After.		Before.	After.		Before.	After.		
3	7,600	7,150	−5·9 (−450)	47	38	−9 (−874)	43	53	+10 (+495)	4	4	0 (−20)	55
12	10,750	9,300	−13·4 (−1,450)	64	46	−18 (−2,630)	31	52	+19 (+1,519)	4	2	−2 (−242)	54
15	7,000	6,300	−10 (−700)	43	51	+8 (+203)	45	46	+1 (−252)	6	2	−4 (−294)	37
16	8,250	8,000	−3 (−250)	32	31	−1 (−144)	65	62	−3 (−372)	2	3	+1 (+76)	25
17	19,925	19,175	−3·7 (−750)	82	79	−3 (−1,229	15	15	0 (−135)	3	5	+2 (+355)	44
18	9,500	7,050	−25·7 (−2,450)	61	51	−10 (−2,225)	34	40	+6 (−430)	3	6	+3 (+135)	—
20	8,175	7,450	−8·8 (−725)	67	74	+7 (+49)	28	21	−7 (−714)	3	3	0 (−21)	42
21	13,850	14,000	+1·0 (+150)	81	71	−10 (−1,238)	14	26	+12 (+1,708)	5	3	−2 (−270)	46
22	6,300	7,000	+11·1 (+700)	64	73	+9 (+1,082)	29	23	−6 (−217)	6	3	−3 (−168)	39
28	10,400	9,500	−8·6 (−900)	70	74	+4 (+250)	21	17	−4 (−569)	7·5	7·5	0 (−68)	60
29	14,400	15,100	+4·8 (+700)	71	78	+7 (+1,554)	15	13	−2 (−197)	13	8	−5 (−664)	51
44	9,150	8,800	−3·8 (−350)	60	64	+4 (+142)	28	25	− 3 (−362)	10	9	−1 (−123)	50
52	6,200	6,150	−0·8 (−50)	47·5	54	+6·5 (+376)	38	40·5	+2·5 (+134)	14	4·5	−9·5 (−592)	53
Average			−5% (−502)			−0·5% (−360)			+1·9% (+46)			−1·5% (−146)	

− =decrease. + =increase.

type, but he did not peel (in the opinion of the skin specialist, Major Betley, it was not scarlet fever). After 2 days quinsy developed; the day following there was severe pain in the left shoulder and left side of neck, and marked restriction of movement. Two days later marked improvement set in, the neck muscles being quite mobile, but there was some residual stiffness in the left shoulder. The temperature rose to 101 and the pulse to 120. The specimens of blood were taken during the attack in the neck and shoulder. He subsequently recovered completely.

Cases of fibrositis (the results are given in Table II):

Case 1.—A case of infective fibrositis in the muscles of the lower limbs following extraction of septic teeth. There was a strong rheumatic family history, and the patient had been a labourer in a show-ground where he was exposed to the weather.

Case 5.—Fibrositis of the sacro-spinal and lower thoracic regions which cleared up with injection of local anæsthetics.

Case 6.—There was pain in the muscles of the neck extending towards the right shoulder with myalgic areas along the borders of the trapezius muscle. He had had previous similar attacks at the same time of the year; these lasted 7 to 15 days, and usually cleared up without specific treatment.

Case 10.—Case of left-sided sciatica of peri-neuritic type.

Case 11.—Case of left lumbar fibrositis complicated by hyperthyroidism; there was mild exophthalmos and palpitation—the thyroid gland itself showed generalised enlargement.

Cases 23, 24, 25 and 26 were all cases of active fibrositis of the muscles in the lumbar region. All had tender areas in the regions involved and radiographic examinations showed no bony changes.

Rheumatoid arthritis (Table II):

Case 30 was a case of active rheumatoid arthritis in a female, age 42, with 2½ years' service. The lesion had started 18 months ago in the left knee followed by both hands. At present there is gross deformity in the hands, but no immobility in the wrist-joints. The sedimentation rate for the first hour was 27.

Osteo-arthritis (Table III):

Case 7 was a case of osteo-arthritis of the left sub-astragaloid joint in a regular soldier. He had had rheumatism in both feet for years, but his temperature and sedimentation rate were normal.

Cases of chronic meningococcal septicæmia (Table III).

Five cases of this condition were seen during the period of the test—that is, these cases were without meningeal involvement. All had positive blood-cultures and all were sent in as cases of "acute rheumatism." This type of case is an exceedingly important one for such a test on account of its close simulation of rheumatic conditions and the dramatic response to

TABLE II.—CASES OF RHEUMATIC DISEASES

Case. No.	Total White Cells per c.mm.		Decrease or Increase per Cent. per c.mm.	Polymorphs per Cent.		Decrease or Increase per Cent. per c.mm.	Lymphocytes per Cent.		Decrease or Increase per Cent. per c.mm.	Monocytes per Cent.		Decrease or Increase per Cent. per c.mm.
	Before.	After.		Before.	After.		Before.	After.		Before.	After.	
Cases of Fibrositis :												
1	11,250	11,000	−2·1 (−250)	65	55	−10 (−1,230)	30	39	+9 (+930)	2	4	+2 (+226)
5	7,500	7,300	−2·6 (−200)	55	46	−9 (−767)	31	39	+8 (+522)	8	4	−4 (−308)
6	8,200	8,400	+2·4 (+200)	58	67	+9 (+872)	36	26	−10 (−768)	6	4	−2 (−156)
10	8,800	7,000	−20·8 (−1,800)	50	43	−7 (−1,390)	45	51	+6 (+390)	4	2	−2 (−212)
11	11,000	8,500	−22·7 (−2,500)	47	67	+20 (+525)	50	32	−18 (−2,830)	2	1	−1 (−135)
Average			−9·1% (−910)			+0·6% (+398)			−1% (−507)			−1·4% (−117)
Case of Rheumatoid Arthritis :												
30	3,350	3,250	−2·9 (−100)	52	53	+1 (20)	36	36	0 (−36)	11	9	−2 (−76)
Cases of Sciatica :												
23	6,970	7,100	+1·8 (+130)	70	69·5	−0·5 (+55)	26	24·5	−1·5 (−73)	3	5	+2 (+46)
24	6,550	6,770	+3·3 (+220)	51·5	57	+5·5 (+485)	43·5	37·5	−6 (−1,511)	3·5	3·5	0 (+7)
25	7,520	7,100	−5·5 (−420)	68	65·5	−2·5 (−463)	27	28·5	+1·5 (−7)	4	4	0 (−14)
26	8,220	8,120	−1·2 (−100)	65	67·5	+2·5 (+138)	30	26	−4 (−355)	4·5	4·5	+1 (+77)
Average			−0·4% (−42)			+1·25% (+51)			−2·5% (−486)			+0·7% (+29)

− =decrease. + =increase.

sulphanilamide therapy. It can only be differentiated with certainty from rheumatic conditions by blood cultures assisted by agglutination and complement-fixation tests. We believe that this condition is much more prevalent than is generally appreciated, and also that the " diplococcus rheumaticus " of Poynton and Paine which was found in some cases of acute rheumatism by these workers was really a meningococcus.[4] These cases are quite indistinguishable clinically from rheumatic conditions.

Kennedy[5] in an interesting paper discusses four cases of chronic meningococcal septicæmia and stresses a possible specific relationship between a rash-like erythema nodosum and meningococcal infections. In his first case there is a history of illness extending over two years and four months. There were periodic temperature remissions from an evening temperature of 103°-104°. Sweating was marked. There was a rash similar to erythema nodosum which appeared in crops and might disappear and reappear in the course of a day. A Gram-negative diplococcus was recovered from the blood—it was rather delicate and died before identification could be established. The patient subsequently died from a purulent meningitis, but cultures from the base of the brain were negative.

Case 2 appeared to be an atypical case of cerebro-spinal meningitis from the beginning in that the onset was a feeling of giddiness, headache, and pain at the back of the neck. Three days later the left foot swelled up and spots appeared on the left leg. Salicylates were given. Fresh crops of spots kept recurring. A meningococcus was isolated from the blood. He subsequently developed gross meningeal symptoms and the cerebro-spinal fluid was turbid but negative on culture. He ultimately recovered.

Case 3 was a young soldier with rigors; a rash appeared first on the flexor surfaces of the arms and extended to the abdomen, chest and extremities; this rash in places was pustular. The diagnosis was erythema nodosum, and salicylates were given. The symptoms were strongly suggestive of acute rheumatic fever —severe generalised pains accompanied by a rise of temperature— and appeared to be relieved by salicylates. Blood cultures were negative.

Case 4 also appeared to be an atypical case of cerebro-spinal meningitis with onset of " wanted to vomit any minute." Two

TABLE III.—NON-RHEUMATIC CONDITIONS

Case No.	Total per c.mm. Before.	Total per c.mm. After.	Decrease or Increase per Cent. per c.mm.	Polymorphs per Cent. Before.	Polymorphs per Cent. After.	Decrease or Increase per Cent. per c.mm.	Lymphocytes per Cent. Before.	Lymphocytes per Cent. After.	Decrease or Increase per Cent. per c.mm.	Monocytes per Cent. Before.	Monocytes per Cent. After.	Decrease or Increase per Cent. per c.mm.
	Cases of Meningococcal Septicæmia :											
19	8,000	8,400	+5 (+400)	64	71	+7 (+844)	30	24	−6 (−384	4	5	+1 (+100)
27	13,370	13,760	+2·92 (+390)	81·5	81	−0·5 (−249)	14·5	14	−0·5 (−12)	3·5	4.5	+1·5 (+152)
35	9,500	9,450	−0·52 (−50)	75	70·5	−4·5 (−498)	12	18·5	+6·5 (+599)	9·5	7·5	−2 (−198)
36	6,800	8,300	−5·68 (−500)	56	54·5	−1·5 (−405)	35	39	+4 (+157)	7	5·5	−1·5 (−160)
47	11,750	11,700	−0·42 (−50)	67	69	+2 (+134)	22	28	+6 (+702)	10	3	−7 (−819)
	Average		+0·26% (+48)			−0·9% (−35)			+2% (+217)			−1·6% (−185)
	Case of Acute Tonsillitis :											
34	12,100	11,120	−8·2 (−1,000)	60·5	59	−1·5 (−771)	29·5	32·5	+3 (+38)	5	5·5	+0·5 (+5)
	Cases of Enuresis (4 Cases done ; Average of Results) :											
37 40 41 42	7,225	7,030	−2·7 (−195)	59	55·1	−3·8 (−349)	33·3	36·5	+3·87 (+208)	5·6	5·1	−0·5 (−50)
	Case of Subacute Osteo-myelitis :											
14	11,250	9,875	−12·2 (−1,375)	57	51	−6 (−2,240)	37	43	+6 (+70)	5	4	−1 (−188)
	Case of Osteo-arthritis :											
7	6,750	4,800	−28·9 (−1,950)	52	45	−7 (−1,324)	42	49	+7 (−462)	5	4	−1 (−142)
	Normal Controls and Gastric Cases (15 done ; Average of Results) :											
	7,833	7,576	−2·12 (−240)	57·1	56·3	−0·8 (−180)	35·03	36·2	+1·2 (−30)	5·9	5·3	−0·6 (−47·2)

− =decrease. + =increase.

Average results of groups—cases of rheumatic disease : Total white cells −4·3 per cent. (−388 per c.mm.), polymorphs +0·58 per cent. (+27 per c.mm.), lymphocytes −0·4 per cent. (−245 per c.mm.), monocytes −1·0 per cent. (−37 per c.mm.).

Average results of groups—cases of non-rheumatic disease : Total white cells −8·97 per cent. (−785 per c.mm.), polymorphs −3·3 per cent. (−816 per c.mm.), lymphocytes +3·84 per cent. (+6·8 per c.mm.), monocytes −0·7 per cent. (−101 per c.mm.).

days later again "felt very sick and weak in the legs as if he might drop down"; there was a slight sore throat, headache across the forehead, aching of legs and arms, and papular spots over surface of tibia. He was put on salicylates and appeared to improve. Symptoms recurred sixteen days later, when a meningococcus was isolated from the blood stream. He subsequently recovered.

Cases 2 and 4, in the light of our experience during the epidemic of cerebro-spinal meningitis two years ago, we would put in the category of infection of the meninges. In such the meningeal symptoms may be slight and transient, yet the cerebro-spinal fluid shows gross turbidity.

Case 3 is the story of a chronic meningococcal septicæmia such as we are meeting with at the present time, and in which we hoped this test would be of material assistance.

Stott and Copeman,[6] with the assistance of bacteriology, have described this condition in the B.E.F. in France during 1940. These writers point out that a remarkable feature of these cases is the feeling of well-being even after an illness lasting many months.

This type of case may appear to respond to salicylates, but a similar result can and does occur with rest in bed without medication. It has been our experience lately that such cases of chronic meningococcal septicæmia are still prevalent in the absence of any increase in the number of cases of cerebro-spinal meningitis beyond the odd sporadic case.

Such cases are discussed here on account of their significance, beyond any reasonable doubt, in any consideration of the rheumatic diseases.

Acute tonsillitis:

Case 34 was a case of acute tonsillitis followed by acute cervical adenitis necessitating admission. He had had "rheumatic" pains in the past. The case was included on account of the association between infection of the tonsillar region and rheumatic manifestations. On admission his temperature was 101 but his pulse was normal.

Case 14 was a case of osteo-myelitis with a subacute flare-up of a chronic lesion of some 14 years' duration in the right tibia. A swelling appeared several times a year, discharged for a few days and then healed spontaneously. Seven days before the test he had been operated on. The temperature and pulse were slightly raised. Osteo-myelitis is a lesion which may and does simulate rheumatic conditions fairly closely, and a differential test would be of considerable value.

Average results of groups—cases of non-rheumatic disease: Total white cells —8·97 per cent. (—785 per c.mm.), polymorphs —3·3 per cent. (—816 per c.mm.), lymphocytes +3·84 per cent. (+6·8 per c.mm.), monocytes —0·7 per cent. (—101 per c.mm.), lymphocytes —0·4 per cent. (—245 per c.mm.), monocytes —1·0 per cent. (—37 per c.mm.).

As controls the authors and 13 patients were used, comprising cases of enuresis (4), internal derangement of knee-joint (2), and 7 dyspeptics. In the last group some were functional and in others a definite organic lesion was present. The results are grouped together and the average taken.

The counts were all taken with the patients in a fasting condition and at rest. Twenty-five of them were done at 12.00 hours—*i.e.*, prior to the mid-day meal—and they had had no food since 07.00 hours of the same day. In the other 25 the specimens were taken at 17.00 hours, and in no case was the period since the last meal less than 4½ hours. Most of the cases were men—a feature inseparable from our present position—but females were also included as the opportunity occurred.

In addition to the total white cells differential counts were taken at the same time—200 white cells being counted. The figure for polymorphs, lymphocytes and monocytes are also given, as it was thought that if an appreciable change were found it would be interesting to see in which type of cell the change actually occurred.

In the cases of acute and subacute rheumatic conditions some showed an increase, others a decrease; the average of these 13 cases in the total white cells is a drop of −5 per cent. (502 per c.mm.); the differential figures in the polymorphs show a drop of −0·5 per cent. (360 per c.mm.); the lymphocytes an increase of +1·9 per cent. (46 per c.mm.), and the monocytes a drop of −1·5 per cent. (14·5 per c.mm.). With one exception none of the cases show a diminution of 15 per cent. 30 minutes after the injection. The exception (case 18) was undoubtedly a case of an active rheumatic lesion following streptococcal infection of the tonsillar region. Some of the cases show an increase (cases 21, 22 and 29).

In the fibrositis and sciatic groups similar results were found—sometimes an increase, other times a decrease. In only 2 cases was there a diminution of over 15 per cent.: (i) case 10—a perineuritis of the sciatic nerve; and (ii) case 11—fibrositis in the region of the lumbar muscles.

In the cases suffering from meningococcal infections without meningeal involvement a similar result was obtained—sometimes an increase, sometimes a decrease. The case of acute tonsillitis—a lesion often associated with the rheumatic conditions—showed

a negative result. The control cases gave similar findings—similar in their inconsistency.

It is to be noted that the greatest diminution (−28·9 per cent.) (case 7) occurred in a non-rheumatic condition.

The total white cell count may vary considerably during the daytime in the normal diurnal tides, and this could quite easily be a factor in such a test. The personal factor also comes in—the difference of a few per cent. is not to be unexpected.

Conclusions

Such a test in its results requires to be specific and consistent if it is to be of value. The findings in this series, which, though small in numbers, includes cases of typical acute rheumatic disease, do not confirm those of the original investigator, and the test, therefore, does not help in the diagnosis of rheumatic diseases. We have found it to be negative in cases of frank rheumatic disease and positive in cases of non-rheumatic conditions, and we submit that it is not a specific one for rheumatic diseases; this confirms Professor Lenoch's warning against making a diagnosis of "rheumatic joint pains" or "myalgia" with the aid of the test.

It is a pleasure to us to record our appreciation of the co-operation of Colonel H. E. Edwards, R.A.M.C., and of the assistance of Sergeant T. Bury, R.A.M.C.

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FIVE HUNDRED CASES OF MYALGIA IN THE BRITISH ARMY

By MICHAEL GOOD

Judging by textbooks muscular diseases are very uncommon, but this is hardly in harmony with the fact that the musculature —the active locomotor apparatus—is the largest organ of the body. According to Sir Colin Mackenzie (1930) the animal body contains not less than 434 muscles, which constitute about 45 per cent. of the total weight, and the musculature contains about one-third of the total blood (R. J. S. McDowall, 1938). Further, one has to bear in mind that the muscles are subject for the greater part of the day to wear and tear, and from a purely theoretical point of view the muscles may be expected to be very liable to disease.

Muscular diseases are very frequent indeed, but their recognition has been delayed probably owing to the fact that they give rise to referred or heterotopic (D. Waterston) pain. This fundamental fact regarding muscle physiology has been studied very recently—experimentally (Sir Thomas Lewis and I. H. Kellgren, 1938) and clinically (Good, 1938). The commonest muscular disease is myalgia, and is present in and responsible for pain complained of by the vast majority of people suffering from what is generally called rheumatism, and in a number of other minor diseases. Myalgia is a disease, the cardinal symptom of which is pain associated with more or less disturbance of function. Since the disturbance of function—*e.g.*, locomotion—is solely due to pain, which is aggravated by contraction of the affected muscle or muscles, myalgia may be looked upon as the prototype of the disease of pain (*La maladie de la douleur*, R. Leriche, 1932).

In such conditions pain is the outstanding symptom, but it is a subjective phenomenon; local tenderness, too, is solely subjective. Experience has shown that there exist normosensitive, hypersensitive and hyposensitive individuals or patients with regard to pain, indicating that the threshold of pain differs individually. In the case of myalgia the diagnosis can be based on objective phenomena.

Definition.—Myalgia is a muscular disease localised in well-definable parts of a muscle and in its appendages—tendon,

ligaments, perimysium, fascia—corresponding anatomically to the origin, insertion, the course or the edge of a muscle. It may affect one (monomyalgia) or several muscles (polymyalgia), and is characterised by the following symptoms:

Subjective Signs—1. *Character of Pain.*—A dull aching, sometimes agonising pain, occurring in attacks of a few minutes' duration or longer, with long intervals. The pain phenomena consist of two kinds—a deep pain, which cannot be localised properly, and a superficial type, which is localised, at least approximately, by the patient. The pain is aggravated by contraction and relieved by relaxation of the affected muscle or muscles. Sometimes it increases during sleep to such a pitch as to awaken the patient. Often pain or aching comes on in the early morning, when starting work, and slowly passes off.

2. *Heterotopicity of Pain.*—The painful areas as described by the patient are of a referred character, and therefore misleading with regard to the localisation of the diseased muscle.

3. *Neuralgic Symptoms.*—Paræsthesia; numbness, pins-and-needles are often complained of, especially in hands and fingers or feet and toes.

4. *Disturbed Function.*—Diminished or temporary loss of power in a special muscle or muscle group—*e.g.*, dropping things from hands or giving way of knees. A very frequent complaint is stiffness, which seems to be akin to diminished strength of a muscle or muscle group.

The objective signs centre round what may be termed "myalgic spots," well and objectively defined areas at the origin, insertion, along the edge or in the course of a muscle, which as a rule are harder to the touch than the surrounding parts. Well-defined nodules may or may not be felt in the substance of the muscle (not to be confused with rheumatic subcutaneous nodules).

Objective Signs.—1. Pressure on a myalgic spot elicits a severe and agonising pain, which is often similar in character and extent to the spontaneous pain complained of.

2. Pressure on such a spot produces wincing pain associated with an involuntary movement—*e.g.*, jerking of head or shoulder in a part of the body, not pressed upon, or the patient "makes a face." This sign is pathognomonic.

3. The myalgic spots, of which the patient is absolutely

unaware, do not coincide with the painful skin area complained of, and in fact are often far removed from it.

4. In the area of referred pain, the skin is often hyperalgesic to pin-pricks and light pressure—*e.g.*, from a hot-water bottle.

5. After appropriate treatment, applied to myalgic spots only, the local pain elicited by pressure, as well as the referred pain, disappears.

From a clinical point of view three different kinds of myalgia may be distinguished—viz.:

(*a*) *Rheumatic* myalgia, giving rise to pain referred to those parts of the body which are subject to rheumatism.

(*b*) *Traumatic* myalgia—cases where the complaint can with certainty be traced to a recent or previous injury, usually of an indirect nature.

(*c*) *Idiopathic* myalgia is of unknown origin and rather vaguely defined by negative criteria; it causes severe pain or ache in some parts of the body—heart, abdomen, feet, many forms of so-called neuritis—which are not supposed to be subject to rheumatism, nor due to an injury.

Myalgia may be an (1) acute, (2) subacute, or (3) chronic disease.

It must be borne in mind that both rheumatoid arthritis as well as osteo-arthritis are not rarely, and rheumatic fever commonly, associated with myalgic conditions in the muscles near to, or even at a distance from, the affected joints. Rheumatic myalgia, provided it is properly diagnosed and accurately located, is a disease which can be cured with certainty. For practical purposes it appears sufficient to describe here only the myalgias of those muscles which are most commonly affected.

Referred Pain from Muscle.—Before proceeding to the description of special myalgias the pain phenomena accompanying this very frequent muscular disease must be described. The most important point is that a diseased muscle, like a diseased viscus, may give rise to referred pain; this is conditional for the understanding of the symptomatology and the diagnosis of myalgias. From my experience as a patient I can say that the pain phenomena consist of (1) a deep dull pain, which as a rule cannot be localised by the patient, and (2) a more superficial pain or paræsthesia, which may be localised, at least approximately. The latter is heterotopic or referred in character, is often localised far away from the affected

muscle, especially in the thigh, and follows a segmental pattern. Clinical observations made over hundreds of cases have shown that pain, as mapped out by the patient himself, is delineated at least approximately on skin areas supplied by segments of the spinal cord—so-called dermatomes—and as a rule originates in muscles supplied by the *same* segments. This rule of dermatomes, although only approximately true, enables us to locate the myalgic spots in the muscles causing the pain or ache or stiffness complained of. The cutaneous areas of the skin innervated by the different spinal nerves are shown in Fig. 1. The localisation of the myalgic spots in the muscles most commonly affected is shown in Fig. 2.

Clinical Features of some Important Myalgias—*Trapezo-Myalgia* (*Myalgia of Neck*).—Pain is usually referred to the neck and shoulder, but sometimes to the occiput extending to the top of the head. The skin areas of referred pain are C2 to C4. Pain is aggravated by movements of the trapezius and relieved by its relaxation. Trapezo-myalgia causes acute and subacute stiff neck and shoulder ache (case 1); sometimes it is responsible for occipital headache (case 2). It is usually rheumatic, but can often be traced to a trauma. It is noteworthy that giddiness is sometimes due to this form of myalgia: idiopathic myalgia of the trapezius, giving rise to muscular vertigo (case 3).

Case 1.—Acute myalgia of trapezius:

November 15, 1941.—Driver H. (29) complained of dull ache in the nape of the neck, aggravated by movements of head or coughing. Myalgic spots (Fig. 3) located in both trapezii and injected with 6 c.c. of 1 per cent. procaine: immediate relief of pain, so that movements of head were practically painless.

November 17.—Slight pain in left shoulder still present; 3 c.c. injected.

November 19.—No complaints.

November 24.—Returned to duty.

Case 2.—Occipital headache:

July 9, 1941.—Gunner G. (20) complained of headache referred to the nape of the neck and extending to the top of the head, for a fortnight (Fig. 4). After injection of 3·5 c.c. of procaine into myalgic spots on both sides of the trapezius, immediate relief of pain. When seen a month later, he was without complaint.

Case 3.—Muscular vertigo:

June 16, 1941.—Private J. (26) has been complaining of dizziness for a fortnight. The dizziness occurs especially when getting up from a lying or bending position. Two myalgic spots in each trapezius were located and injected (5 c.c. of procaine).

June 18.—No dizziness. Not reported sick again in the following 2½ months.

Omomyalgia (*Myalgia of Shoulder*).—Pain is usually referred to C4-5, rarely also to C6. Movements of shoulder are restricted, active and passive movements are extremely painful. This myalgia often simulates arthritis, periarthritis or bursitis of shoulder. Often the malady is of traumatic origin.

CASE 4.—Shoulder myalgia (Fig. 5):

November 10, 1941.—Gunner N. (22). For about 2 years pain and dull ache in both shoulders, occurring in attacks and improved by rest. Since a month pains have become much worse. Admitted to hospital for periarthritis. Myalgic spots in both trapezii and biceps tendons injected (6 c.c. of procaine): immediate relief of pain and restoration of movements.

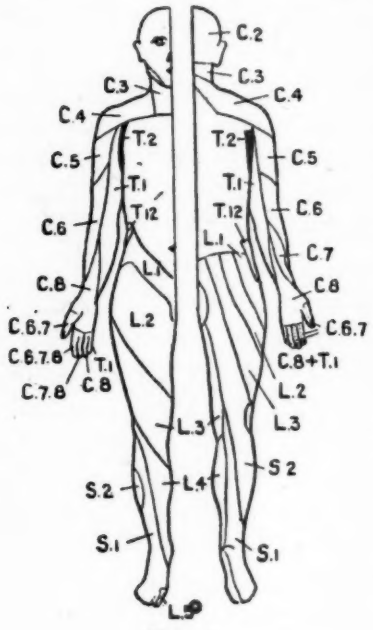

FIG. 1.

November 13.—1 c.c. of procaine injected. Returned to duty on November 19 after he had been without complaint for a week.

CASE 5.—Myalgia of shoulder and arm (Fig. 6):

November 12, 1941.—Gunner B. (30). Has been suffering for last 6-7 weeks from stiffness and pain in right shoulder and arm, worse at night and early morning. After 4 weeks of radiant heat treatment slight improvement, but very soon pain became worse. Myalgic spots in long head of biceps and heads of extensors of hand and fingers, injected (2·5 c.c. procaine).

On discharge (November 17, 1941) he said spontaneously: "The treatment has been wonderful."

CASE 6.—Traumatic myalgia of shoulder (Fig. 7):

June 10, 1941.—Lieutenant R. (23). Fell on elbow the day before. Complained of severe pain in left shoulder and arm. Movements of shoulder and arm very restricted and extremely painful; 2·5 c.c. of procaine injected into myalgic spots located in long head of biceps.

June 12.—Pain still present; 3 c.c. injected into insertion of trapezius to scapula and one spot of biceps. Full relief of pain. Returned to duty June 16.

June 27.—No complaints.

Myalgia of Elbow (*Cubital Myalgia*).—Pain is referred to outer aspect of arm and hand and first to third fingers (external myalgia) or to the inner aspect of arm and hand and third to fifth fingers (internal myalgia). Myalgic spots can be located in the heads of extensors or flexors of wrist and fingers or in both.

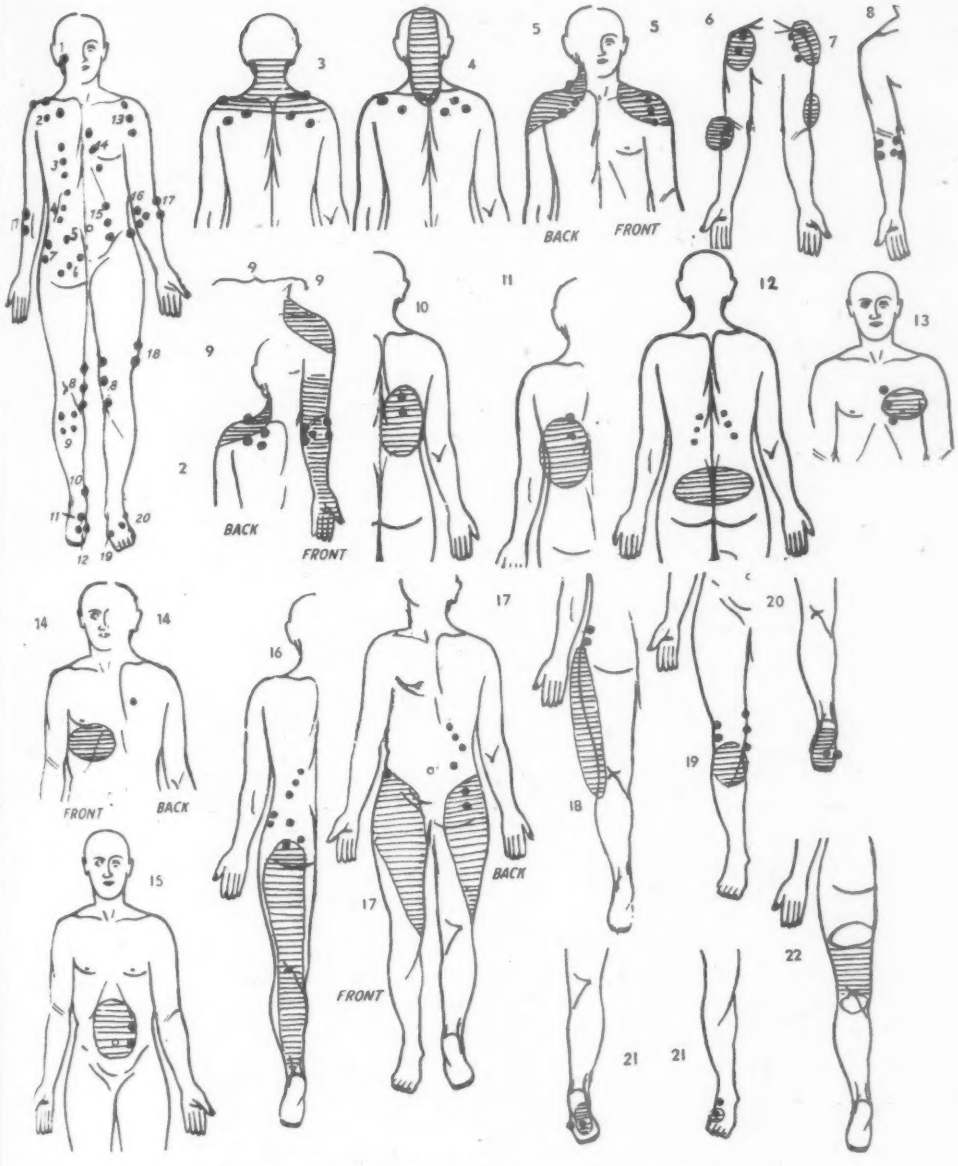

FIG. 2.—MYALGIC SPOTS AND AREAS OF REFERRED PAIN.

The numerals in the following key refer to the figure in the diagram at the top left-hand corner; in the other figures the horizontal lines indicate the areas of pain as mapped out by patients and the dots the myalgic spots.

1. Sternomastoid.
2. Trapezius.
3. Sacrospinalis.
4. Quadratus lumborum.
5. Gluteus medius.
6. Gluteus maximus.
7. Tensor fasc. lat.
8. Semimembran.-tendin.
9. Gastrocnemius.
10. Tendo Achilles.
11. Flexor digitor. brev.
12. Flexor hallucis brev.
13. Biceps tendon.
14. Pectoralis major.
15. Rectus abdominis.
16. Flexors } of wrist and
17. Extensors } fingers.
18. Lateral vastus.
19. Abductor hallucis.
20. Peroneus brevis.

Sometimes the origin of the brachioradialis is also affected, and simulates what is often diagnosed "brachialgia." Cubital myalgia often gives rise to paræsthesia—pins-and-needles, numbness, etc.—and temporary loss of or diminished power—*e.g.*, dropping things from hands—and may be present in and responsible for some cases of peripheral neuritis.

CASE 7.—Idiopathic myalgia of elbow (Fig. 8):

November 8, 1941.—Private S. (22). A year ago he developed pain in dorsum of right wrist and weakness of the forearm. The arm was strapped for 3 months and later kept in plaster of Paris for 5 months. No bony changes were found radiologically. Last 3 months he received massage and electrical treatment. On admission he complained of pain on dorsum of wrist and weakness of forearm and fingers, "no power of gripping." Myalgic spots were located in heads of extensors and flexors of hand and injected with 4 c.c. of procaine.

November 9.—1 c.c. injected into extensors. On physical training and remedial exercises.

December 12.—Discharged to duty. He reported 14 days later, when he was without complaint.

CASE 8.—Idiopathic myalgia of shoulder and elbow ("brachial neuritis"):

December 2, 1941.—Sergeant H. (37) was treated for brachial neuritis at P. Hospital from August 6 to October 31, at convalescent home from October 31 to November 21, and readmitted to P. Hospital November 21. His reflexes were normal; sensation left arm: light touch negative, pin-pricks almost negative, heat and cold much diminished; Wassermann and Kahn negative. X-ray normal apart from slight rarefactions. He had been treated with massage, electricity, and betain (injections + tablets). On admission to the Military Hospital he complained of severe pains in left shoulder and anterior surface of arm (Fig. 9). Myalgic spots were located in left trapezius and extensors and flexors of arm.

December 3.—Injection of 6 c.c. procaine into myalgic spots, movements of shoulder, arm and fingers appear normal and painless.

December 8.—"45 per cent. improved." 4 c.c. of procaine injected. On physical training and remedial exercises.

December 24.—Still complains of pain. Examination: no myalgic spots. Seen by psychiatrist, who diagnosed psychogenic pain.

January 2, 1942.—On questioning he agrees that he has improved up to 80 per cent. Objectively: movements of shoulder and arm appear normal.

January 7, 1942.—Discharged to duty.

Dorsal and Lumbar Myalgias.—Pain is referred to the back below scapular spine down to the lumbar region, or to the small of the back. Pain is aggravated by stooping, bending and inspiration. Myalgic spots in the outer edges of the sacro-spinalis on one or both sides may be responsible for high backache and for pleurodynia. Dorsal myalgia often simulates

intercostal neuralgia and neuritis. In lumbago the myalgic spots are regularly found in the border of the quadratus lumborum, generally on the right and left, rarely they are only found on one side. The procaine injections in lumbago are best given in a tangential direction from the flanks, the patient sitting on a locker, with legs hanging down and arms crossed, but not supported by legs.

Case 9.—Dorsal myalgia (Fig. 10):

August 19, 1941.—2nd Lieut. P. (28), for 6 months stabbing sharp pain in back, worse on lying down and getting up. Myalgic spots in sacrospinalis located and injected (3 c.c.).

August 20.—50 per cent. improved. One more spot injected (1·5 c.c.). Pain fully relieved.

August 21.—Reported to say that he is cured.

Case 10.—Dorsal myalgia, simulating intercostal neuralgia:

July 13, 1941.—Gunner N. (29). Referred to me by his medical officer as suffering from intercostal neuralgia. Complains of pain corresponding to D6-7 on right, pain aggravated by inspiration. Two myalgic spots on outer edge of right sacrospinalis injected: immediate relief of pain.

July 15.—Reported cured.

Case 11.—Dorsal myalgia (Fig. 11):

August 12, 1941.—Gunner S. (27) complains of backache on left side; 3 c.c. injected into sacrospinalis with immediate relief of pain.

August 14.—Reported to have no complaints.

Case 12.—Lumbar myalgia (lumbago):

December 25, 1941.—Major —— has been suffering from lumbago for several months. Treated by radiant heat and massage, apparently with little relief; he was unable to localise his pain. Myalgic spots in right quadratus lumborum and one spot in right gluteus medius. Injected (10 c.c.): pain immediately and greatly relieved ("up to 90 per cent.").

December 31.—No complaints.

January 16, 1942.—Ditto.

Case 13.—Lumbago (Fig. 12):

November 12, 1941.—Pioneer W. (40) has been suffering from backache for last 3 months. Admitted because pain much worse last 3 days. Myalgic spots in quadratus lumborum on both sides injected (5 c.c.): pain immediately relieved, relaxation of cramped lumbar muscles.

November 19.—5 c.c. injected. On physical training.

November 26.—3 c.c. injected.

December 2.—On discharge no complaint for last week.

Precordial Pain.—Heart pain complained of by patients with a normal cardiovascular system is, as a rule, of muscular origin. Muscular pain referred by the patient to the heart may also be present in some organic diseases of the heart (M. G. Good, 1940). Two forms can be distinguished:

(*a*) Mammary pain. Pain is referred to a skin area—usually oval in shape—above or round the nipple, mostly on the left,

but sometimes on the right side. The myalgic spots are as a rule found in the origin (ligamentous part) of the sterno-costal part of the pectoralis major near the sternum, in the third to fifth intercostal spaces.

(*b*) Inframammary pain. Pain is referred to an oval skin area below the nipples—right or left—sometimes also across the costal arch and upper part of the hypochondrium. Myalgic spots are localised in the outer edge of the sacrospinalis (right or left), and rarely in the origin of the pectoralis major from the lower ribs.

Both types of what is called by patients heart pain are aggravated by deep breathing. Patients are therefore inclined to develop a type of shallow breathing.

CASE 14.—Left mammary pain (myalgia of pectoralis major) (Fig. 13):

May 9, 1941.—Gunner C. (30) complains of heartache for a fortnight, worse on breathing; 4 c.c. injected into myalgic spots at origin of pectoralis major: immediate relief of pain, even on deep inspiration.

May 12.—Heart pain gone. Not reported again.

CASE 15.—Right infra-mammary pain (Fig. 14):

July 28.—Gunner B. (29) complains of "heart pain" for a week. Pain referred to an area below right nipple. One spot in right sacrospinalis injected (2 c.c.) with instantaneous relief of pain.

July 30.—Reported to have no complaint.

Rectus Myalgia (*Myalgia of Abdomen*).—This form of myalgia is of great practical importance, since it gives rise to pain referred to the upper and/or lower abdominal region on the right or left, thus may simulate a visceral disease of the abdominal cavity. A very characteristic, almost pathognomonic feature is the point that pain is aggravated by bending and/or lifting heavy weights. The myalgic spots are usually localised in the outer border of the rectus abdominis in its upper or lower parts. It often is of unknown (idiopathic) origin, but sometimes can be traced with certainty to a trauma.

CASE 16.—Myalgia of rectus abdominis:

May 23, 1942.—Gunner T. (29) has been complaining of pain along left costal margin; treated with strapping, a contusion of rib being assumed to be responsible for the symptom.

May 26.—Not improved. Myalgic spot in left rectus located and injected (2 c.c.).

May 28.—50 per cent. improved. Two more spots in outer edge injected (1·5 c.c.). Pain fully relieved.

May 30.—Reported no complaint.

CASE 17.—Rectus myalgia, simulating gastric disease (Fig. 15):

November 30, 1941.—Private D. (32). Since a boy of 10 he suffered from pain in stomach, especially after heavy meals—fish or greasy food. Attacks occurred every 2-3 months, lasting for a few days or sometimes 3-4 weeks. Attacks occurred when he happened to be in a depressed mood. About 7 weeks ago, after having been detained in barracks, he developed stomach pain, starting an hour after meals—fish or fried food—lasting for varying periods. Pain increased on lifting heavy weights. X-ray of stomach and other tests were negative. Two myalgic spots located in left rectus abdominis and injected with 2 c.c. of procaine.

December 17.—Discharged to full duty, after his gastric complaints had been absent for 14 days.

Sciatica (*a Myalgia of Hip*).—The syndrome of sciatica is in the vast majority of cases caused by a polymyalgia of hip muscles (coxal myalgia). The myalgic spots are, as a rule, localised in the quadratus lumborum, glutei and tensor fasciæ latæ. Muscular sciatica seems to be a suitable designation of this form of the malady, in contrast to true or nervous sciatica, which in my experience is rare. The explanation of the fact that a myalgia of the hip muscles just mentioned causes pain referred to the posterior aspect of thigh and leg is apparently due to the rule of dermatomes: the quadratus lumborum is supplied by L1-4, gluteus maximus by L4-5 and S1-2, gluteus medius and tensor fasciæ latæ by L4-5 and S1—viz., segments of the cord supplying the posterior aspect of the leg (Fig. 1). Muscular sciatica can be cured with certainty by appropriate injections of procaine into the accurately located myalgic spots. It is noteworthy that in hip myalgia pain may be referred to thigh and groin only, although the myalgic spots are almost the same as in sciatica.

Case 18.—Sciatica due to hip myalgia (Fig. 16):

November 8, 1941.—Driver B. (36). Sciatic pain in left leg for last 7 months; treated at a C.C.S. hospital for 6 weeks with heat and massage Slight improvement. Pain much worse of late. Examination: Lasègue's sign positive on left, ankle jerk absent on left; myalgic spots located in quadratus lumborum, glutei and tensor fasciæ latæ and injected with 5 c.c. of procaine: pain immediately disappeared and movements of left leg were painless.

November 10.—Complained of pain over left calf. Two myalgic spots in gastrocnemius injected (2·5 c.c.).

November 13.—No pain although on physical training.

Up to his discharge (November 28) he was treated for moderate hyperpiesis, but sciatic pain was absent since last injection.

Case 19.—Sciatica (Fig. 17):

November 12, 1941.—Sergeant M. (37). Suffered from malaria (1932) and twice from sciatica 1 and 2 years ago respectively. Admitted to hospital

for right sciatica. Treatment with aspirin and radiant heat only slightly improved.

November 26.—Transfer to rheumatism ward. Examination: well-developed scoliosis; on standing he puts body weight to left leg. Lasègue's sign positive. Reflexes normal. Myalgic spots located in quadratus lumborum, glutei and tensor fasciæ latæ injected (6 c.c. of procaine), After injection the quadratus lumborum, which was cramped before, relaxed and patient could touch toes without discomfort.

November 29.—Pain on anterior aspect of leg still complained of and slight scoliosis still present; 5 c.c. of procaine in right quadratus lumborum and gluteus medius injected.

December 4.—No complaint, but quadratus lumborum still contracted; 2 c.c. injected.

December 6.—After injection of 2 c.c. muscle fully relaxed. On physical training.

December 17.—Return to duty. *August* 15, 1942.—No complaints.

Case 20.—Sciatica:

Surgeon Lieutenant (36). Septic tonsillitis and rheumatism—fibrositis and arthritis of spine—some years ago. For a week severe agonising sciatic pain in right leg. After injection of 6 c.c. of procaine into tensor fasciæ latæ and gluteus medius instantaneous relief of pain. Next day he noticed slight discomfort at site of injection. Pain did not recur during following 3 months.

Myalgia of Tensor Fasciæ Latæ.—Monomyalgia of this muscle is often due to an injury, usually of an indirect nature. The myalgic spots are generally found in the origin from the anterior superior spine and the border of its upper muscular part at the outer aspect of thigh. Pain is referred to the outer aspect of legs and is greatly increased on standing, walking or bracing the injured leg. The results of procaine injections are often very remarkable.

Case 21.—Traumatic myalgia of tensor fasciæ latæ (Fig. 18):

May 14, 1941.—Gunner O. (29). Kicked leg a fortnight ago while playing hockey. Three days later he developed pain at outer aspect of right leg, unable to walk. After injection of 3 c.c. into origin of tensor fasciæ latæ instantaneous relief and restoration of movement. He played hockey 2 days after treatment, to his and his sergeant's great surprise. I saw him a fortnight later, when he had no complaint whatsoever.

Myalgia of Knee.—This is a very common malady. Pain is referred to a circular or oval area round or below the patella, or rarely to the popliteal space. The myalgic spots are localised in the border of the lower half of the semimembranosus-tendinosus and sometimes also in the lateral edge of lower part of vastus lateralis. Myalgia of knee is present in many diseases which are often diagnosed arthritis, osteo-arthritis, chronic synovitis, etc. In doubtful cases procaine injection may be used as a diagnostic

test to prove conclusively that a given pain and disturbance of movements are of muscular origin. In addition, it may be found that the treatment leads to a rapid cure, provided objectively defined myalgic spots, but not just "tender spots," said to be painful on pressure by patients, are thoroughly injected.

CASE 22.—Myalgia of knee (Fig. 19):

June 25, 1941.—Pilot Officer P. (53). For the last 20 years rheumatism in both knees. A few weeks ago treated at a naval hospital for arthritis with no improvement. Examination: distinct creaking in left knee on movements. Myalgic spots in semimembranosus-tendinosus on both sides and in vastus lateralis of left knee; 5 c.c. of procaine injected (left knee).

June 27.—No pain in left knee; 3 c.c. injected into right knee.

June 28.—"Very pleased; never felt so well in whole life."

CASE 23.—Traumatic myalgia of knee:

May 31.—Sergeant H. (26). 2½ months ago he suffered from locking of right knee, due to an injury. He was operated on (removal of cartilage). Since the operation he has been suffering from pain in knee, especially on walking. He was seen by the orthopædic surgeon, who diagnosed "chronic synovitis," and his discharge from the Army was under consideration by a Medical Board. A myalgia of knee was detected. After injection of 5 c.c. of procaine into semimembranosus-tendinosus muscle there was immediate relief of pain and restoration of function.

June 7.—No complaint. Three weeks later he appeared before the same Board and said that he had been on full duty since the treatment and had no complaints whatever. He was categorised A1.

Painful Feet (*Myalgia of Foot*).—This condition is extremely important from the military point of view. Many men report sick because of the syndrome of painful feet. The complaints are of a dull ache or burning pain on the plantar or dorsal surface of the foot, on standing, and especially on marching. From a recent publication of Capt. R. T. Burkitt (1941) I cite the following sentences: "The condition of flat-foot in all its varying degrees is by far the commonest cause of doubtful efficiency. The 'severe' form in which the head of the talus has gone right over and the flatness is 'complete' causes least trouble. Some men with this condition are placed in a category barring them from an infantry regiment. Of those who are not the majority have no trouble with their feet at all; they can perform long route marches. . . . It is a recognised fact that the severest pain is always caused by the high arched foot beginning to give way. . . . Any case which fails to respond to treatment (*i.e.*, conservative M. G.) within three weeks should be 'boarded out' without delay." The author mentions the interesting fact that in his battalion 30 men

reported sick with symptoms caused by fallen arches. But there were 33 other men in the same unit with a marked degree of flat-foot, as evidenced by footprints and appearance, who never complained although they had been for route marches. The results of 30 treated cases were: "17 probable failures out of 26 followed-up cases"—*i.e.*, 65·39 per cent. failures.

From my own experience in the Army I can confirm Burkitt's view: complaints of painful feet are mostly due to flat-feet, but sometimes to pes cavus. Moreover, many officers and other ranks never complain of foot troubles in spite of fallen arches. From this fact one must, in my opinion, draw the conclusion that falling of the arches may be neither the cause nor the origin of the syndrome of painful feet. In all the cases examined by me (about 40 cases) an objectively definable disease—myalgia—of foot muscles could be ascertained. The myalgic spots are usually localised in the course, or mostly in the insertion, of flexor brevis hallucis, the insertion of the Achilles tendon to the calcaneum and the flexor brevis digitorum in the middle of its course. Here, too, the injection of procaine into the accurately located myalgic spots serves as a diagnostic test, which proves conclusively that the pain complained of is of a referred nature and of muscular origin. The following short case-histories will show that procaine injection is a simple and reliable method which enables us to control pain permanently and restore function in a short time.

CASE 24.—Myalgia of foot (Fig. 20):

June 21, 1941.—Gunner I. (21). Complained of pain in feet, especially on standing and marching. Examination: pedes plani, myalgic spots at the insertion of flexor brevis hallucis. Right foot injected (2 c.c.).

June 23.—No pain in right foot. Left foot injected (3 c.c.).

June 25.—No complaints; not reported again, although ordered to do so if pain recurred.

CASE 25.—Myalgia of foot (Fig. 21):

June 26, 1941.—Bombardier B. (25). Complained of pain under right foot. Arch normal, but myalgic spots at insertion of flexor brevis hallucis located and injected (2 c.c.).

June 27.—80 per cent. improved; myalgic spots at insertion of peroneus brevis injected (2 c.c.).

June 28.—No pain.

June 30.—No complaints.

Aggravation and Simulation of Pain.—Under present extraordinary conditions of a nation in arms, it has to be borne in mind that complaints may be exaggerated or even simulated, because they may subconsciously—or in case of a malingerer

consciously—be intended to serve a special purpose. Looked at from a psychological point of view, such a behaviour of a soldier or factory worker can be understood, although not approved of (" tout comprendre, n'est pas tout pardonner," under abnormal conditions !). Psychologically it can be understood that a soldier or worker who has been doing a tricky, dirty or generally unpleasant job dreams of a temporary break and of a peaceful rest in a hospital. Small wonder, that he may subconsciously be inclined to aggravate a slight or moderate pain, which he happens to feel, in order to excuse himself before his conscience for trying to shake off temporarily or for a longer period his duties towards his country.

The modern diagnosis of myalgia is based on objective criteria which, I think, enable us to distinguish with great probability or with certainty between a genuine complaint and exaggerated or simulated symptoms. The characteristic signs are:

(1) Delineation of pain: glove and stocking types of pain, or pain extending round a whole limb.

(2) Pseudo-myalgic spots. If a pressure is exercised on an area of supposed referred pain, but not a myalgic spot, the patient gives a jerking of a part of his body. Moreover, this reaction is exaggerated—*e.g.*, the jerking is repeated several times—and delayed—*i.e.*, a few seconds elapse before the reaction occurs. During the time interval one distinctly feels a voluntary contraction of one or several muscles situated round the pressed-upon area. In contrast to that, the reaction of a genuine patient is immediate and consists of one jerk only. But a necessary precaution is to demonstrate to the patient the difference between a " sharp pain " elicited by pressure on a true myalgic spot and a pain produced by the same pressure on a normal muscle or bone. It must be emphasised that a diagnosis of exaggeration or simulation of pain should be made only after several very thorough examinations have led to the same result; and if there is any doubt the patient should be given the benefit of it.

Case 26.—Simulation of pain (Fig. 20):

July 9, 1941.—Gunner T. (32). Complains of pain of a stocking type between knee and middle of upper leg. A very thorough examination did not reveal any myalgic spots. In addition the man showed a repeated and exaggerated jerking of head on pressure on quadriceps or patella. He was returned to duty and did not report sick again in the next 6 weeks.

The cases referred to in this article were seen by me partly at a main dressing station and several medical inspection rooms

and partly in a rheumatism ward of a military hospital. The vast majority were treated very successfully by procaine injections; a small percentage of the cases refused this treatment. Table I shows the distribution of myalgias over the different regions of the body, classified under the heading of rheumatic, traumatic and idiopathic. In the table all sciatica cases are included under myalgias of hip, the conditions of painful feet under idiopathic myalgias of leg, unless a traumatic origin could be ascertained. It is interesting to note that myalgia of leg was the most frequent malady, next in frequency were the myalgias of hip, dorsal+lumbar region, and neck, diminishing in that order.

TABLE I.—STATISTICS (500 CASES).

	Number of Cases.			*Total.*
	Rheumatic.	*Traumatic.*	*Idiopathic.*	
Myalgia of:				
Neck	38	10	12	60
Shoulder	22	8	1	31
Arm	13	20	2	35
Dorsal and lumbar	93	9	4	106
Hip	**100**	9	—	109
Leg	37	**46**	**44**	**127**
Chest	—	2	8	10
Abdomen	—	9	13	22
Totals	303	113	84	500

A very interesting fact emerging from Table II, which shows the frequency of individual muscle involvement, is that the quadratus lumborum and trapezius are most frequently diseased, next in frequency being tensor fasciæ latæ, glutei, semimembranosus tendinosus and sacrospinalis, in that order. No myalgias were met with in the triceps, the adductors and extensors (except lateral vastus) of the leg. An explanation of the frequency of myalgias of the first seven muscles of Table II is suggested by distinguishing between two functions of a muscle. E. Bramwell (1925) has drawn attention to this distinction when dealing with primary muscular dystrophies. This author states that the distribution of muscular involvement in muscular dystrophies suggests that muscles which are of special importance as fixators in relation to maintenance of posture are predisposed; whereas muscles more especially concerned with active purposive movements, of which we are more directly conscious, are either spared

or affected only at a later date. It would appear that this explanation holds good also for the relative high incidence of involvement of quadratus lumborum, trapezius, sacrospinalis and tensor fasciæ latæ, which, to a large extent, are fixators. According to Bramwell the muscles of the thigh play an important part as fixators in running. Probably the semimembranosus tendinosus plays a similar and equally important rôle as a fixator of knee.

TABLE II.—FREQUENCY OF INDIVIDUAL MUSCLES INVOLVED.

No.	*Muscle.*	*Number of Cases.*	*Per Cent.*
1	Quadratus lumborum	**158**	31·6
2	Trapezius	**122**	24·4
3	Tensor fasciæ latæ	**84**	16·8
4	Gluteus medius	**70**	14·0
5	Gluteus maximus	**64**	12·8
6	Semimembranosus tendinosus	**58**	11·6
7	Sacrospinalis	**55**	11·0
8	External cubital	27	5·4
9	Internal cubital	25	5·0
10	Rectus abdominis	25	5·0
11	Biceps humeri	24	4·8
12	Flexor brevis hallucis	24	4·8
13	Peroneus brevis	21	4·2
14	Gastrocnemius	20	4·0
15	Vastus lateralis	18	3·6
16	Tendo Achillis	14	2·8
17	Pectoralis major	12	2·4
18	Peroneus longus	8	1·6
19	Deltoid	6	1·2
20	Abductor hallucis	5	1·0
21	Flexor brevis digitorum	4	0·8
22	Sternomastoid, brachioradialis (each)	2	0·4
23	Sartorius, gracilis, anconeus (each)	1	0·2

N.B.—Every muscle was counted only once, even if both sides were affected.

ETIOLOGY AND PATHOLOGY.—The primary cause (or causes) of rheumatic myalgias is not known. But in the opinion of most clinicians the following factors play a rôle as an exciting cause: 1, septic foci; 2, allergic conditions; 3, climatic conditions; 4, endocrine dysfunction (thyroid, sex glands); 5, trauma; and 6, mental worries and emotional strain. In my opinion 7, an "autonomic imbalance," either in the form of predominance of the sympathetic—sympathicotonia—or of the parasympathetic—vagotonia—and probably also 8, an imbalance

of electrolytes, especially of the Na : K : Ca ratio, may be important contributing factors. Experience in the Army has shown that in a great number of cases—22·6 per cent. of all cases as shown in Table I—myalgias could with certainty be traced to a recent or previous injury.

The pathology of myalgias is at present very obscure. R. Stockman (1920) has described the pathology of "nodules" which he took to be responsible for fibrositis. Stockman found that the "nodules" consist of inflamed white fibrous tissue and that the small blood vessels often show very distinct thickening of all their coats, as if they had suffered from the action of an irritant. But it is necessary to point out that in the majority of myalgias "nodules" are conspicuous by their absence. In my experience a hard nodule is often found in the heads of the flexors of wrist and fingers in cubital myalgia. But in other cases the myalgic spots are harder to the touch than the surrounding—*i.e.*, the muscular area is in a spastic condition. This can best be seen in lumbago, where the quadratus lumborum is contracted; on appropriate injection of procaine the muscle relaxes almost instantaneously. Moreover, nodules in the substance of a muscle are often found in healthy subjects who have no complaints whatever. In my opinion the conclusion is justified that nodules are generally not responsible for myalgic conditions. In a recent publication (1942) E. J. Moynahan and E. S. Nicholson confirm that "nodules were not a constant feature of the malady clinically: they are absent more often than not." For this very reason fibrositis is by no means an adequate term for the malady, which is a muscular disease, localised in anatomical parts of a muscle (Good, 1938). If an inflammatory condition were present it should be termed interstitial myositis. But since the inflammatory process is very much in doubt, it would appear more appropriate to call it for the present myalgia or myopathy of rheumatic, traumatic or idiopathic origin. It is a fact that injection of 1-2 c.c. of 1 per cent. procaine abolishes the myalgic spot definitely and permanently. But it is extremely unlikely that a local anæsthetic will cure an inflammatory process in a muscle or any other organ without delay.

On the other hand the common denominator of the contributory factors of myalgia mentioned above may be looked for in a disturbance of the local blood supply. As a work-

ing hypothesis the conception of a diminished blood supply confined to the myalgic areas is tentatively put forward, leading to oxygen want—local hypoxæmia or hypoxia—which would account for the characteristic symptoms of myalgias—viz., pain, paræsthesia and loss of power (Good, 1938). Such a "vasomotor disequilibrium" (Leriche, 1930) may be brought about by stimulation of vaso-constrictor sympathetic fibres. It is noteworthy that adrenaline, the action of which is often identical to stimulation of the sympathetic, has a dual effect on the blood vessels of the muscles, which are dilated by small doses and constricted by large ones (McDowall, 1938). R. Pemberton (1935) has put forward the same conception of disturbed circulation for articular rheumatism and brought forward evidence in support of this view.

TREATMENT.—A rapid, effective and permanent cure can be obtained by injections of procaine into the myalgic spots.

Solution used:

℞	Procaine	1·0 grm.
	Phenol	0·5 „
	Saline	ad 100·0 c.c.

S.: Sterile in rubber-capped bottle.

Technique.—The myalgic spots are mapped out on the skin with a blue dermatograph, the pencil marks painted over with iodine and 1-2 c.c. of 1 per cent. procaine solution injected intramuscularly into each spot, care being taken to infiltrate the whole myalgic area. The result of a thorough and accurate injection are: (1) almost instantaneous relief of pain; (2) relaxation of the spastic muscle, as evidenced by palpation; and (3) pressure on the myalgic spot no longer elicits pain or produces a wincing or involuntary jerking. In this way marvellous, sometimes fantastic results are obtained, which must appear almost incredible to those who have not used the method or seen its effects. Few things in clinical medicine can be more dramatic than to obtain in a patient, who is in agony and doubled up, an almost instantaneous relief of pain and restitution of the disturbed function of the diseased muscles after injection of procaine. But a proviso has to be added—these extremely favourable results will not be obtained by injection of spots tender to pressure—*i.e.*, the patient complains of pain on pressure, a "subjective" sign only. Moreover, sensitiveness to pain differs very much individually, as mentioned above. A myalgic spot objectively located and

once properly injected no longer gives rise to complaints. A myalgia can be and often is cured by one treatment; if complete cure is not obtained, it is due to one of the following reasons: (1) not all myalgic spots were injected; (2) a faulty technique with regard to location of myalgic spots or injection; or (3) exaggeration of pain by patient.

Owing to lack of space the theory of the procaine effect—*i.e.*, why a local anæsthetic should relieve permanently pain arising from a myalgic spot cannot be discussed here. The discussion of this question, which is intimately connected with the theory of pain, would require a special article.

TABLE III.—ANALYSIS OF 230 CASES OF MYALGIA.

Treated. 214		*Not Treated.* 15		*Under Treatment.* 1	*Total Number.* 230
reported 140	not reported 74	refused 13	simulation 2		
cured 134	not cured 6				

The analysis refers to cases I have seen in a place, somewhere in England, where I was posted for a longer period and was in a position to verify the results. Of the 230 officers and other ranks who suffered from myalgias 15 received no treatment, mostly because injections were refused; a few of these men were markedly improved after one or two injections, but refused further treatment on the ground that in their opinion the injections did not do them any good; 2 men were given no treatment because I was satisfied that their complaints were not genuine.

Of the remaining 214 cases, who were treated by procaine injections only, 134 reported "cured"—*i.e.*, they had no symptoms, pain or disturbance of function; 6 men reported "not cured"—*i.e.*, some had, although improved, still symptoms, and a few said they had derived no benefit from the treatment. All these cases were given a very thorough examination, and I was satisfied that the symptoms were exaggerated. They were returned to full duty and have not reported sick again in the next one to three months; 74 cases have not reported after the last treatment, although ordered to do so. On enquiry the medical

officers concerned confirmed that the men had not reported sick again. Taking an unprejudiced view it may be assumed that the 74 not-reported cases were cured, or at least so much improved that the men did not think it worth while to report again, though 5 men reported sick after one to three months with the same complaints, but were cured by one or two or more treatments. Among the cases were 26 of foot myalgia; the results of procaine injection were as follows: 4 men refused the treatment; of the 32 officers and other ranks treated 13 reported cured, and 9 men did not report after the last treatment, although ordered to do so in two days.

Summary

Myalgia is a very frequent disease localised in certain anatomical parts of one or more muscles. Its characteristic features are "myalgic spots" which can be located by objective criteria and give rise to referred or heterotopic pain. Myalgia is present in and responsible for the vast majority (according to statistics 95 per cent.) of patients suffering from rheumatism; it is not rarely associated with rheumatoid arthritis, osteo-arthritis, and commonly with rheumatic fever. The malady is also responsible for a number of minor diseases which can be traced to an injury —traumatic myalgia. It is often of unknown origin—idiopathic myalgia—and mimics visceral and nervous diseases (heart pain, neuralgia or neuritis, sciatica, syndrome of painful feet, etc.). The localisation of the myalgic spots—the characteristic features of myalgias of neck, shoulder, arm, back, lumbar region, hip and leg—is described. Procaine injection into the accurately and objectively located myalgic areas is warmly recommended as relieving pain and other complaints in a most dramatic way and as leading to a rapid cure.

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EMPIRE RHEUMATISM COUNCIL

SIXTH ANNUAL REPORT

MY LORDS, LADIES AND GENTLEMEN,

IN submitting the Annual Report for 1942, I express again my regret that it has been considered inadvisable by the War Emergency Committee to convene the Annual Meeting. To have asked our members, some 150 in number—practically all engaged in work of national importance, and many living at a distance from the metropolis—to meet in London would have been a trespass on energy which must be conserved for the effective prosecution of the war.

Our President, H.R.H. the Duke of Gloucester, acknowledging the Report for 1941, expressed his pleasure that "thanks to prompt action in sending out missions of enquiry to the Rheumatism Treatment Centres of America and Europe before the outbreak of war, you are now able to present a plan of treatment based on the international as well as British practice." He also warmly welcomed the close connection established with the American Rheumatism Association, writing: "In this field of humane effort, as in so many others, the best hope for the world rests with the friendly co-operation of the English-speaking peoples."

Another development in the integration of our war on rheumatism is to be recorded—the conclusion of an agreement with the British Orthopædic Association. This can contribute greatly to the efficiency of practitioners in the diagnosis and treatment of crippling conditions caused by rheumatic diseases and also to national economy. A joint policy was unanimously agreed at a conference of representatives of both bodies in June. It is as follows:

1. The Empire Rheumatism Council and the British Orthopædic Association are in cordial agreement that their mutual co-operation in the diagnosis, prevention and treatment of crippling conditions will be of the greatest service to the health of the community.

2. Both bodies aim at close *liaison* between the physician specialising in rheumatism and the orthopædic surgeon, seeking to enlist the sympathetic co-operation of the general practitioner, the Public Health services and social workers generally.

3. Orthopædic hospitals and orthopædic departments of general hospitals should include on their medical staffs a physician with special knowledge of the rheumatic diseases.

4. Rheumatism centres should include on their medical staffs an orthopædic surgeon.

5. Since the application of methods of physical therapy and of occupational therapy for orthopædic and rheumatic patients is largely identical, a joint out-patient clinic should, wherever practicable, serve for both classes of patients. In such joint centres the orthopædic cases will be under a team headed by an orthopædic surgeon and for rheumatic cases the team will be headed by a physician.

6. In view of the growing appreciation of the importance of regionalisation of medical services the scheme for rheumatism treatment centres should be planned to fit into such schemes as may be arranged for the future. This has, in fact, already largely been done in orthopædic schemes.

7. As in orthopædic work the development of successful centres has been based upon the legal requirements of the notification of certain crippling diseases, and upon the public responsibility for the provision and payment for their treatment, so in Rheumatic Disease a similar degree of responsibility should be assumed by the State or Local Authority.

8. Adequate provision for the training of young physicians and surgeons in research, diagnosis and treatment should be associated with suitable encouragement to make the study of Rheumatic Diseases a lifework.

9. To put into effect the agreed plan of co-operation a Joint Standing Advisory Committee should be constituted of equal, or nearly equal, numbers of representatives of both organisations, with a secretariat of two, one from each organisation.

The Standing Advisory Committee has been constituted as follows: Lord Horder, G.C.V.O., F.R.C.P. (Chairman); Mr. G. R. Girdlestone, F.R.C.S. (Vice-Chairman); Hugh Burt, M.R.C.P. (acting for Lieut.-Col. Copeman, F.R.C.P.); Norman Capener, F.R.C.S.; W. A. Cochrane, F.R.C.S.; Squadron-Leader W. D. Coltart, F.R.C.S.; Prof. L. S. P. Davidson, F.R.C.P., Ed. and Lond.; A. G. Timbrell Fisher, M.C., F.R.C.S.; S. L. Higgs, F.R.C.S.; Brig.-Gen. F. D. Howitt, C.V.O., F.R.C.P.; Prof. H. J. Seddon, F.R.C.S. Joint Secretaries: Norman Capener, F.R.C.S., and Sir Frank Fox, O.B.E.

There is provision for the co-option of other members and for varying the personnel of the Committee and its secretariat.

Research

In this field progress continues in spite of the checks imposed by war conditions.

The Director of our Naval Research Foundation, Dr. C. A. Green, has been granted temporary honorary rank of Surg. Commander, R.N.V.R., a recognition of the value of his work which is highly appreciated and which will help him in his task. His term of engagement with the Empire Rheumatism Council has been further extended, as also has been that of Professor Ernst Freund (West London Hospital Section). Additional generous donations from the Sir Halley Stewart Trust and Mr. Frederick A. Pearson will assist in financing these extensions. Ultimately, some of the expense of the Foundation may fall upon the general fund of the Council, but the results already achieved and the good promise for the future demand its continuance.

Dr. C. B. Dyson continues his research effort in County Durham.

Clinical research work has been carried on (1) to find if any "specific" diagnostic tests for the rheumatic condition exist; (2) to estimate the value and appropriate dosage of gold salts in the treatment of certain rheumatic conditions; (3) to test the efficacy of a method of treatment regarding which favourable results have been reported from a provincial hospital. No definite conclusions can yet be announced. Such clinical tests, to be of value, call for strict control and much patient observation.

Treatment

There has been encouraging progress in this very important part of our campaign. "Rheumatism: A Plan for National Action" continues to hold professional and public attention. Grounds for confidence exist that the Plan will be accepted at least as the basis for discussion of national action in post-war health policy. Intimations from responsible authorities, national and municipal, in various quarters of the United Kingdom justify the hope that the near future will see our community equipped with such effective means for the prevention and treatment of rheumatism as our admirable Public Health Services provide for other of the greatly prevalent diseases.

Applications for the translation rights of the Plan of Treatment in Spanish and Polish have been received and granted without asking for any copyright fee. The purpose of the publication is educational, not profit-seeking. Its accounts, however, show a present small credit with promise of a larger one. I have decided that any profit should go to the Council's funds. A third edition was published in January and future reprints probably will be necessary. The circulation to date has been nearly 6,000 copies.

The Royal Canadian Army Medical Corps is giving attention to the treatment of rheumatic sufferers in the Canadian Expeditionary Force. Major Douglas Taylor of that Corps has asked for the assistance of our Council in this matter. He took a prominent part in the work of the Canadian Rheumatic Disease Association (which is affiliated with our Council). All possible help will be given. As members are aware, the "Plan of National Treatment" outlined in an appendix a method of organising treatment for rheumatism by an Army in the Field.

The British Spas have been carrying on a campaign during the course of the year, the object of which is to emphasise that their healing resources are not fully utilised. Responding to a request from Mr. John Hatton, Chairman of the British Spas Federation, "for advice and help," I have outlined the views of our Council as to the part the Spas can usefully take in the War on Rheumatism. With a recognition that they are not at present utilised to the full extent possible and desirable, the points I impressed were: (1) that Spa treatment should be available to all sufferers for whom competent medical advice judges it neces-

sary; (2) that Spa authorities should shape their policy to provide for people of little means; (3) that regional allocation of patients to the Spas is wise for reasons of economy in travelling, but there should be an over-riding medical allocation if some Spa is judged most suitable for a particular type of case. I suggested that the Spas could usefully engage at present in a special survey of their medical staff arrangements and expressed the opinion that—if this is not already the case—every Spa should have on its consultant (or permanent) medical staff at least one physician with a specialised knowledge of the Rheumatic Diseases and one orthopædic surgeon.

The American Congress of Physical Therapy, 1941, granted to our Hon. Medical Secretary, Lieut.-Col. Copeman, a Gold Key award for his work on Rheumatism with the B.E.F. in France, "in developing a remarkable physical therapy organisation in the Field under the most unfavourable conditions." This recognition by our American colleagues is welcome. The importance of Lieut.-Col. Copeman's work was in its practical demonstration of what has been our constant theme: that Rheumatism Treatment need not be vastly expensive nor depend for effectiveness on elaborate apparatus.

Increased pressure on the services of the very few treatment centres situated within the industrial areas of the kingdom is again to be recorded. As before noted, some of the Spa institutions are not fully utilised, but, valuable as is the part they can take in regard to rheumatism treatment, obviously they cannot meet the needs of the many thousands of sufferers who require means of treatment near to their homes. Citing the experience of centres with which the Empire Rheumatism Council is in close touch, the Red Cross Clinic, London, reports a constantly increasing demand, over-taxing its present accommodation. The Clinic of the Order of St. John, London, reports to the same effect (it has the advantage of being able to refer those requiring in-patient accommodation to the arthritic unit of St. Stephen's L.C.C. Hospital). The clinic at the West London Hospital, established in 1938 by our Council in co-operation with the boroughs of Fulham, Hammersmith and Kensington, has made great progress; the number of patients treated has risen by 50 per cent. since 1939, and the medical staff has been increased from two to six; this clinic also has the advantage of being able to send severe cases to an E.M.S. Hospital for in-patient treat-

ment. Other treatment centres in England and Scotland report full utilisation of their services.

The position, however, still remains that to the great majority of sufferers no facilities for appropriate treatment are available. Yet, as the statistics of clinics show, a proportion of about 60 per cent. of sufferers get cure or substantial relief if given the right treatment at an early stage, and this without serious disturbance of their industrial or domestic life.

Administration

The Council will wish to concur in an expression of high appreciation of the good care which has been given to our affairs by the members of the War Emergency Committee—viz., Dr. C. W. Buckley, Lieut.-Col. W. S. C. Copeman, A. G. Timbrell Fisher, Dr. Mervyn H. Gordon, Col. the Rt. Hon. John Gretton, Brig.-Gen. F. D. Howitt, Sir Walter S. Kinnear, T. W. Robinson, H. Gordon Thompson, and Dr. Hugh Burt. The last has been co-opted to the Committee whilst acting for the hon. medical secretary, now absent from the kingdom on service abroad. Every call on their time has been cheerfully met. My medical colleagues, I know, will agree with me in giving special mention to our three lay members, the Rt. Hon. John Gretton, Sir Walter Kinnear, and T. W. Robinson. A great source of strength to the Council has been the assiduous help of these gentlemen of administrative and financial ability. To our organising secretary, Sir Frank Fox, with his vision and unique experience, we cannot be too grateful or express too much appreciation.

The Official Journal

Our Official Journal maintains its high scientific standard. Articles published represent now in almost equal proportion British and American work on the problems of rheumatic disease. Members of the Council are urged to help its circulation among the medical profession and laymen interested in public health.

The Future

The urgent task for the near future will be the organisation of an adequate scheme of post-graduate education in rheumatic disease. I fervently hope that it may be timed for 1943, with the war ended and the nations of good intent facing with sober

faith the serious task of "winning the peace." Not the least part of that task will be the pursuance of a courageous policy of "social medicine," one aspect of which will be our special care. In that effort, "Wisdom is the principal thing. . . . Wisdom cometh, length of days in her right hand." There will be need to foster a more intensive study of the rheumatic diseases, both in respect of causation and treatment, in the medical profession, in the realm of administration, and also among the people so that they, too, may contribute the essential element of self-help.

(*Signed*) HORDER.